Appointment

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 5/5/2020 1:08:51 PM
To: Burneson, Eric [Burneson.Eric@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
CC: Khera, Rajiv [Khera.Rajiv@epa.gov]

Subject: Perchlorate Response to Comments
Attachments: Consolidated Perchlorate Draft Comment Response Document 5-4-20.egb.docx
Location: Microsoft Teams Meeting

Start: 5/5/2020 6:00:00 PM
End: 5/5/2020 6:30:00 PM
Show Time As: Busy

I would like to discuss the comments I have provided thus far on the perchlorate RTC document and provide an opportunity for you to ask any questions about comments to date.

Join Microsoft Teams Meeting

Ex. 6 Personal Privacy (PP) United States, Washington DC (Toll)

Conference ID: Ex. 6 Personal Privacy (PP)

Local numbers | Reset PIN | Learn more about Teams | Meeting options

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Appointment

From: Townsend, Clifton [Townsend.Clifton@epa.gov]
Sent: 2/23/2017 4:21:33 PM
To: Townsend, Clifton [Townsend.Clifton@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Huff, Lisa [Huff.Lisa@epa.gov]; Olson, Daniel [Olson.Daniel@epa.gov]

Subject: Update on Perchlorate Occurrence Report
Attachments: POMR Brief.pptx
Location: DCRoomEast2418/DC-ICC-OW-OGWDW

Start: 2/27/2017 3:00:00 PM
End: 2/27/2017 3:45:00 PM
Show Time As: Busy

Good day all,

I am setting up a quick meeting/briefing to go over some the potential issues/questions that we may face regarding the updating of the Perchlorate Occurrence Report that I feel requires Management input. Specifically the Chambers request to remove additional PWSs from our occurrence analysis as well as the inclusion of newer data that has been reported by the California. Attached you will find a briefing that I put together for your review.

Thanks again

Clifton

Appointment

From: Olson, Daniel [Olson.Daniel@epa.gov]
Sent: 1/25/2017 1:34:26 PM
To: Olson, Daniel [Olson.Daniel@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Flowers, Lynn [Flowers.Lynn@epa.gov]; Hafez, Ahmed [Hafez.Ahmed@epa.gov]; Helm, Erik [Helm.Erik@epa.gov]; jeffrey.fisher@fda.hhs.gov; kinetics@leavens.us; Miller, Gregory [Miller.Gregory@epa.gov]; Schlosser, Paul [Schlosser.Paul@epa.gov]; Strong, Jamie [Strong.Jamie@epa.gov]; Kapraun, Dustin [Kapraun.Dustin@epa.gov]; Georges, Jessica [Georges.Jessica@epa.gov]
CC: Noyes, Pamela [Noyes.Pamela@epa.gov]; Cantilli, Robert [Cantilli.Robert@epa.gov]; Gilbert, Mary E. [Gilbert.Mary@epa.gov]

Subject: BBDR Model Status
Attachments: Untitled Attachment; Untitled Attachment; Untitled Attachment; Untitled Attachment; Untitled Attachment; Untitled Attachment; Untitled Attachment; Untitled Attachment; Untitled Attachment
Location: DCRoomEast2339/DC-ICC-OW-OGWDW; Ex. 6 Personal Privacy (PP)

Start: 1/31/2017 8:00:00 PM
End: 1/31/2017 9:00:00 PM
Show Time As: Busy

Recurrence: Weekly
every Tuesday from 3:00 PM to 4:00 PM

Standing meeting on BBDR model status. Not all people can make all meetings but it is the best time for most people.

Call-in number: Ex. 6 Personal Privacy (PP)
Code: Ex. 6 Personal Privacy (PP)

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 2/12/2020 2:52:57 PM
To: McLain, Jennifer L. [McLain.Jennifer@epa.gov]; Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]; Tiago, Joseph [Tiago.Joseph@epa.gov]
CC: Christ, Lisa [Christ.Lisa@epa.gov]; Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]
Subject: FW: Revised Document
Attachments: Perchlorate Reductions 2-10-20 v2.docx

Attached is the update on systems and perchlorate reductions. The only outstanding system is in LA.

From: Christ, Lisa
Sent: Wednesday, February 12, 2020 9:50 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: FW: Revised Document

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, February 10, 2020 12:37 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Revised Document

Hi Lisa,

We got new information from the MD system. There was some misunderstanding with the information request but here is the latest.

The treatment plant at chapel hill was recently taken off line and it was replaced with new productions wells and treatment plant which started operations in January 27, 2020. Please see the new language that I have incorporated in the revised document below.

"EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that the Chapel Hill WFP was taken off line and it was replaced with a new treatment plant and five new production wells. The new treatment plant started operations on January 27, 2020. System personnel also indicated that monitoring was conducted in November 2019 and the analysis shows that perchlorate was not detected in either the source well water or the finished water."

Thanks
Sam

==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Monday, February 10, 2020 10:31 AM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Revised Document

Thanks Sam.
Do we know exactly what the contractor asked each PWS? Based on this response: **EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that no follow-up/updated monitoring data for perchlorate is available.** It appears we only asked about monitoring…did the contractor ask about any changes in source water and/or treatment too?

Thanks,
Lisa

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, February 10, 2020 8:14 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: Revised Document

Hi Lisa,

We heard back from the Chapel Hill system in MD and they do not have new data for Perchlorate. The document has been updated accordingly. Please see attached.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 3/16/2020 7:01:55 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
CC: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: FW: EDITS - RE: Revised Perchlorate Briefing Documents
Attachments: Perchlorate Recommendations for PWS_03.16.2020.docx; Perchlorate Reductions_03.16.2020.docx; Decision for Perchlorate Final Regulatory Action_3-13-20_revisedOWIO.docx

Lisa:
Please take a look at the comments/ revisions in the attached and let me know if you would like to have a call to discuss how to incorporate these changes.
Eric

From: Tiago, Joseph <Tiago.Joseph@epa.gov>
Sent: Monday, March 16, 2020 2:53 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Cc: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: FW: EDITS - RE: Revised Perchlorate Briefing Documents

From: Aguirre, Janita <Aguirre.Janita@epa.gov>
Sent: Monday, March 16, 2020 2:49 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>
Subject: EDITS - RE: Revised Perchlorate Briefing Documents
Importance: High

Hi Jennifer,

A few edits from Dave. Please review and confirm. In particular, please address the comment bubbles in the "Perchlorate Reductions" document. Please also review the write-up under #4 in the "Perchlorate Recommendations for PWS" document to confirm that it uses guidance type language, rather than authoritative, regulatory language. Due to formatting, yellow highlights (rather than redline) show changed text.

This is due tomorrow by noon, so please let me know as soon as the edits are incorporated.

Thank you,
Janita

Janita Aguirre – Special Assistant to David Ross and Anna Wildeman
U.S. Environmental Protection Agency | Office of Water | Office of the Assistant Administrator
Phone: **(202) 566-1149** | Email: **aguirre.janita@epa.gov**

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Friday, March 13, 2020 5:34 PM
To: Aguirre, Janita <Aguirre.Janita@epa.gov>

Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>
Subject: FW: Revised Perchlorate Briefing Documents

Janita – your assistance on this is appreciated! Is it possible to provide these revised documents – updated per Dave's input?

Thank you
Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Friday, March 13, 2020 5:28 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Subject: Revised Perchlorate Briefing Documents

Jennifer:
Attached please find a revised Perchlorate Briefing documents. We had submitted a previous versions of these document for OW review along with the Perchlorate Reductions and Recommendations Documents. We have updated these documents while awaiting further comments from OW. The revisions made to the documents are as follows

- The one pager – Decision for Perchlorate Final Regulatory Action – Has been updated in response to Dave's request to incorporate information about the timing of the release of the stipulation to NRDC regarding the consent decree. This document reflects OGC's input.
- The Reductions Document – has been updated to reflect the information we received from the States of Maryland and Ohio regarding the status of the system that previously detected perchlorate at levels greater than 18ppb. We have also added a document number.
- The Recommendations Document has been updated to reflect add a Document Number.

If OW has not yet reviewed the last versions provided we recommend sending these forward to replace the versions awaiting review. If there are comments on the previous versions we can incorporate those prior to sending them forward.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 11/12/2019 2:19:36 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: Revised Briefing Document
Attachments: Option Selection for Perchlorate 11-12-19 v1.docx

Hi Lisa,

The statements were accurate, I made one additional edit in response to your comment. Attached is the revised version of the document.

Let me know if it is ok to share this document with OGC, so that they can start working on their input for the placeholder.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Friday, November 08, 2019 1:39 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: Revised Briefing Document

Hi Sam,
I did some rewording, but want to make sure this is still accurate. Please take a look and make changes as needed.

Thanks,
Lisa

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Friday, November 08, 2019 1:00 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: Revised Briefing Document

Hi Lisa,

Here is the revised document. The edits are highlighted. Let me know if you have any comments or edits.

Thanks
Sam
==========

Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 5/4/2020 12:27:53 PM
To: Parikh, Pooja [Parikh.Pooja@epa.gov]
CC: Wehling, Carrie [Wehling.Carrie@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]
Subject: Request for Review - Draft Perchlorate Response to Comment Document
Attachments: Consolidated Perchlorate Draft Comment Response Document 4-29-20 v1 Clean.docx; Consolidated Perchlorate Draft Comment Response Document 4-29-20 v1 Redline.docx

Hi Pooja,

We are requesting OGC review and clearance of the attached Perchlorate Response to Comment Document. We anticipate that this document will be needed in order to transmit the Withdrawal FRN to OMB. Eric will be reviewing this document concurrently with OGC, and I will let you know if there are any mayor edits as a result of his review.

I have attached a clean version and also a redline version of the document which captures some of your previous comments/edits on the document.

Let me know if you have any questions.

Thank You
Sam

==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 4/15/2020 9:26:48 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: Draft Responses to Comment - Perchlorate
Attachments: Perchlorate Draft Comment Response Report - Lisa C Review 4-15-20.docx

Hi Lisa,

Attached you will find the remaining sections of the comment response document for Perchlorate. For the other sections, which you had already reviewed, I incorporated your suggested edits as well as those from OGC. But I did not include those sections here because it is easier to navigate the document without those more dense sections.

I am still waiting for ORDs input, but all the other sections are coming together nicely. I will need to finalize the Health Effects section to assemble the document because that section cross-references to all other pertinent sections of the response document.

On this file you will see a few comments that are highlighted yellow because I need to make sure that those are appropriately cross-referenced to the Health Effects section. Once I have your input on this file I should be able to quickly assemble the whole document and I will be able to send the final/draft version to you.

Thanks
Sam

==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 3/13/2020 9:27:47 PM
To: McLain, Jennifer L. [McLain.Jennifer@epa.gov]
CC: Tiago, Joseph [Tiago.Joseph@epa.gov]; Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]
Subject: Revised Perchlorate Briefing Documents
Attachments: Decision for Perchlorate Final Regulatory Action_3-13-20_revised. .docx; Perchlorate Recommendations for PWS 3-13-2020.docx; Perchlorate Reductions 3-13-2020.docx

Jennifer:
Attached please find a revised Perchlorate Briefing documents. We had submitted a previous versions of these document for OW review along with the Perchlorate Reductions and Recommendations Documents. We have updated these documents while awaiting further comments from OW. The revisions made to the documents are as follows

- The one pager – Decision for Perchlorate Final Regulatory Action – Has been updated in response to Dave's request to incorporate information about the timing of the release of the stipulation to NRDC regarding the consent decree. This document reflects OGC's input.
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Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 2/10/2020 5:37:24 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
CC: Khera, Rajiv [Khera.Rajiv@epa.gov]
Subject: RE: Revised Document
Attachments: Perchlorate Reductions 2-10-20 v2.docx

Hi Lisa,

We got new information from the MD system. There was some misunderstanding with the information request but here is the latest.

The treatment plant at chapel hill was recently taken off line and it was replaced with new productions wells and treatment plant which started operations in January 27, 2020. Please see the new language that I have incorporated in the revised document below.

"EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that the Chapel Hill WFP was taken off line and it was replaced with a new treatment plant and five new production wells. The new treatment plant started operations on January 27, 2020. System personnel also indicated that monitoring was conducted in November 2019 and the analysis shows that perchlorate was not detected in either the source well water or the finished water."

Thanks
Sam

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Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Monday, February 10, 2020 10:31 AM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Revised Document

Thanks Sam.
Do we know exactly what the contractor asked each PWS? Based on this response: **EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that no follow-up/updated monitoring data for perchlorate is available.** It appears we only asked about monitoring…did the contractor ask about any changes in source water and/or treatment too?

Thanks,
Lisa

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, February 10, 2020 8:14 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: Revised Document

Hi Lisa,

We heard back from the Chapel Hill system in MD and they do not have new data for Perchlorate. The document has been updated accordingly. Please see attached.

Thanks
Sam
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Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 3/17/2020 1:30:06 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]; Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]; Tiago, Joseph [Tiago.Joseph@epa.gov]
CC: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: RE: EDITS - RE: Revised Perchlorate Briefing Documents
Attachments: Perchlorate Recommendations for PWS_03.17.2020.Changes.docx; Perchlorate Reductions_03.17.2020RLSO.docx

Lisa: I have made additional edits to the documents attached to further expand the introduction to the Reductions Document and to address the POU text by describing the option as a Point of Use or Point of Entry Treatment option. Can you/Sam prepare clean versions of these documents so that we are ready for the 10:00 deadline.

Joe, Yu Ting and Jennifer
I am assuming Dave needs to see the mark ups to verify the edits so I am copying you in case you want to review while we are preparing clean versions.
Eric

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Tuesday, March 17, 2020 8:16 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: EDITS - RE: Revised Perchlorate Briefing Documents

Eric, please see the revised document attached. I noticed we were missing references we added on 2/28 so I put those back in the reductions document. I do not agree with a edit on page 2 (highlighted blue) stating POU protects the whole home. Let us know if you'd like additional changes.

Lisa

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, March 16, 2020 4:37 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: EDITS - RE: Revised Perchlorate Briefing Documents

Thanks. Can I get a revised by 8:30 am tomorrow morning?

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Monday, March 16, 2020 3:42 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: EDITS - RE: Revised Perchlorate Briefing Documents

Eric,
I think they are mostly straight forward. If I recall we were asked previously for underlying data for the AZ and NV surface water data, I don't think we have it, but Sam is checking. The questions about storage for hypochlorite should be in the AWWA protocol. Lisa

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, March 16, 2020 3:02 PM

To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FW: EDITS - RE: Revised Perchlorate Briefing Documents

Lisa:
Please take a look at the comments/ revisions in the attached and let me know if you would like to have a call to discuss how to incorporate these changes.
Eric

From: Tiago, Joseph <Tiago.Joseph@epa.gov>
Sent: Monday, March 16, 2020 2:53 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Cc: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: FW: EDITS - RE: Revised Perchlorate Briefing Documents

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From: Aguirre, Janita <Aguirre.Janita@epa.gov>
Sent: Monday, March 16, 2020 2:49 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>
Subject: EDITS - RE: Revised Perchlorate Briefing Documents
Importance: High

Hi Jennifer,

A few edits from Dave. Please review and confirm. In particular, please address the comment bubbles in the "Perchlorate Reductions" document. Please also review the write-up under #4 in the "Perchlorate Recommendations for PWS" document to confirm that it uses guidance type language, rather than authoritative, regulatory language. Due to formatting, yellow highlights (rather than redline) show changed text.

This is due tomorrow by noon, so please let me know as soon as the edits are incorporated.

Thank you,
Janita

Janita Aguirre – Special Assistant to David Ross and Anna Wildeman
U.S. Environmental Protection Agency | Office of Water | Office of the Assistant Administrator
Phone: **(202) 566-1149** | Email: **aguirre.janita@epa.gov**

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Friday, March 13, 2020 5:34 PM
To: Aguirre, Janita <Aguirre.Janita@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>
Subject: FW: Revised Perchlorate Briefing Documents

Janita – your assistance on this is appreciated! Is it possible to provide these revised documents – updated per Dave's input?

Thank you

Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Friday, March 13, 2020 5:28 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Subject: Revised Perchlorate Briefing Documents

Jennifer:
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Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 5/20/2020 1:17:33 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
CC: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: FW: Important: Perchlorate submittal to OW
Attachments: Perchlorate Action Memo 5-19-20.docx; Draft Perchlorate Final Action FRN 5-19-20 v1.docx; Final Perchlorate Action for 12866 Review Transmittal Memo OGWDW to OW 5-19-20.pdf; 12866docketguidelines-09-27-10.pdf

Importance: High

FYI

From: Burneson, Eric
Sent: Wednesday, May 20, 2020 9:08 AM
To: Lousberg, Macara <Lousberg.Macara@epa.gov>
Cc: McLain, Jennifer L. <Mclain.Jennifer@epa.gov>
Subject: FW: Important: Perchlorate submittal to OW
Importance: High

Macara: I understand that WPS are not processing the perchlorate action which is subject to a consent decree deadline because of missing items in the package related to FAR. Since WPS ran the FAR I don't see why this information cannot be added by WPS (note that there is no economic analysis for this final action). It is critical that this action be transmitted to OP ASAP. Thanks for your assistance.

From: Flaharty, Stephanie <Flaharty.Stephanie@epa.gov>
Sent: Wednesday, May 20, 2020 7:38 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Burneson, Eric <Burneson.Eric@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>
Subject: Important: Perchlorate submittal to OW
Importance: High

Good Morning,

There's some confusion in OW over our submittal of the perchlorate docs. for Charlotte's review. Joe asked that I enter the attached documents into CMS (w/o review) for Charlotte. Is this the formal submittal? To initiate OMB Review, we need to follow the Action Development Process checklist (as applicable) and label the FRN per the attached guidance. (Note: submit the FAR memo and associated concurrences in on PDF file.)

Thanks for your timely attention…any questions, please let me know, thanks!

OMB REVIEW OF RULE

Left Side	***Right Side***
□ OGC Concurrence e-mail (or letter) □ Core Workgroup concurrences: emails: ORD, OPEI , OECA □ FAR memo and attached Workgroup FAR concurrences □ Draft Economic Analysis (1 + e copy) * □ Note: Docket Guidelines https://intranet.epa.gov/actiondp/documents/12866docketguidelines-09-27-10.pdf	□ Transmittal Memo from DD to OD □ Transmittal Memo from OD to AA (Orig + yellow) □ Transmittal Memo from AA to OPEI (Orig + yellow) □ Draft Action Memo from AA to Administrator □ Draft Rule and Preamble FRN □Send all Files electronically to IO (SF) – will forward to OP https://intranet.epa.gov/actiondp/adp-templates/index.htm#adp

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 3/13/2020 3:07:06 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: Draft Responses - Health Effects
Attachments: Draft Responses - Health Effects Comments.docx

Hi Lisa,

Here are the draft responses to the health effects comments. I will update responses and check for consistency as soon as we get feedback from ORD. I also sent this document to Greg Miller for his awareness. He told me that he would look at the responses and get back to us if needed.

Thanks
Sam

==========

Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 2/10/2020 1:13:52 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
CC: Khera, Rajiv [Khera.Rajiv@epa.gov]
Subject: Revised Document
Attachments: Perchlorate Reductions 2-10-20 v1.docx

Hi Lisa,

We heard back from the Chapel Hill system in MD and they do not have new data for Perchlorate. The document has been updated accordingly. Please see attached.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 2/18/2020 4:18:38 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
CC: Khera, Rajiv [Khera.Rajiv@epa.gov]; Huff, Lisa [Huff.Lisa@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: 2 perchlorate documents -- for your records
Attachments: Perchlorate Reductions 2-18-20_rk-egb.docx

Thank you Sam and Rajiv for your work to address my comments. I have a few more follow up request in the attached. Can you see if we can get OLEM to expedite their feedback on the table? Putting forward this document is critical to getting decisions needed to make the court filing.
Eric

From: Hernandez-Quinones, Samuel
Sent: Tuesday, February 18, 2020 10:23 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: RE: 2 perchlorate documents -- for your records

Hi Eric, please see attached document. It incorporates your suggested edits and addresses your questions.

I am also waiting for some additional feedback form OSWER on the table they provided, as they way it reads now it appears to show several entries for the same mitigation site. Depending on their feedback we might have to update that table.

Thanks
Sam

==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Huff, Lisa <Huff.Lisa@epa.gov>
Sent: Tuesday, February 18, 2020 10:17 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: 2 perchlorate documents -- for your records

Yes I'll check with Sam and get back to you.

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Tuesday, February 18, 2020 10:07 AM
To: Huff, Lisa <Huff.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: FW: 2 perchlorate documents -- for your records

Lisa:

I sent the attached comments to Lisa Christ on Thursday but I don't think I received a revised document. Since Lisa is out today, can you check with the Team to get me a revised today?
Thanks
Eric

From: Burneson, Eric
Sent: Thursday, February 13, 2020 2:05 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: 2 perchlorate documents -- for your records

Thank You Lisa
I have a few comments/edits on the perchlorate reduction document in the attached.
Eric

From: Christ, Lisa
Sent: Wednesday, February 12, 2020 9:59 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: 2 perchlorate documents -- for your records

Eric – just wanted to put both documents in one place for you. Both have been reviewed by Jennifer and Christina. Lisa

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Wednesday, February 12, 2020 9:53 AM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Subject: FW: Revised Document

Attached is the update on systems and perchlorate reductions. The only outstanding system is in LA.

From: Christ, Lisa
Sent: Wednesday, February 12, 2020 9:50 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: FW: Revised Document

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, February 10, 2020 12:37 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Revised Document

Hi Lisa,

We got new information from the MD system. There was some misunderstanding with the information request but here is the latest.

The treatment plant at chapel hill was recently taken off line and it was replaced with new productions wells and treatment plant which started operations in January 27, 2020. Please see the new language that I have incorporated in the revised document below.

"EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that the Chapel Hill WFP was taken off line and it was replaced with a new treatment plant and five new production wells. The new treatment plant started operations on January 27, 2020. System personnel also indicated that monitoring was conducted in November 2019 and the analysis shows that perchlorate was not detected in either the source well water or the finished water."

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Monday, February 10, 2020 10:31 AM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Revised Document

Thanks Sam.
Do we know exactly what the contractor asked each PWS? Based on this response: **EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that no follow-up/updated monitoring data for perchlorate is available.** It appears we only asked about monitoring…did the contractor ask about any changes in source water and/or treatment too?

Thanks,
Lisa

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, February 10, 2020 8:14 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: Revised Document

Hi Lisa,

We heard back from the Chapel Hill system in MD and they do not have new data for Perchlorate. The document has been updated accordingly. Please see attached.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water

Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Khera, Rajiv [Khera.Rajiv@epa.gov]
Sent: 3/26/2020 8:03:03 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
CC: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: Responses to OGC Comments
Attachments: Draft Perchlorate Compendium HRRCA sections 8-1 to 8-4 rk1-lc.docx .docx

Hi Sam-
Please see attached my responses to OGCs and Lisa's comments. Broadly, **Ex. 5 Deliberative Process (DP)**
Ex. 5 Deliberative Process (DP) All other comments from OGC are totally palatable. Lisa's input was very valuable. Thanks
Rajiv

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Thursday, March 19, 2020 11:08 AM
To: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: FW: Request for OGC Review - Court Filing Perchlorate Communications Plan

Hi Rajiv,

Here is OGCs input regarding the responses to the HRRCA comments. As you will see in their comments it looks like there is a misunderstanding of the process we are taking in informing the withdrawal. We might have to have a call with them in the coming days to have a discussion about how we have done this in the past and how we do not want to set a precedent on involving economic considerations into the Reg Det process.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Parikh, Pooja <Parikh.Pooja@epa.gov>
Sent: Wednesday, March 18, 2020 2:03 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: Request for OGC Review - Court Filing Perchlorate Communications Plan

Sam - please see attached mark-up of the economic assessment comments. Carrie had just a few additional suggestions, which are reflected in the comment bubbles. Please let me know if you have any questions.

Pooja

Pooja S. Parikh
Attorney- Advisor

U.S. Environmental Protection Agency
Office of General Counsel, Water Law Office
Phone: 202 564-0839
Email: parikh.pooja@epa.gov

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Friday, March 13, 2020 1:07 PM
To: Parikh, Pooja <Parikh.Pooja@epa.gov>
Subject: RE: Request for OGC Review - Court Filing Perchlorate Communications Plan
Importance: High

Hi Pooja,

Will you be able to provide your feedback on the Economic Assessment Responses to comments today?

Also, I am working on another batch of comments that I plan to send to you as soon as Lisa is done with her review. I expect that I will be sending that to you very soon. But we would benefit from seeing your feedback on the first set of comments so that we can try to capture any concerns or guidance you might have on subsequent responses.

Thank You
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Parikh, Pooja <Parikh.Pooja@epa.gov>
Sent: Wednesday, March 11, 2020 2:46 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: Request for OGC Review - Court Filing Perchlorate Communications Plan

Hi Sam –

Apologies but I've been caught up on other matters and haven't had a chance to finish reviewing the Economic Assessment Responses to Comments. I will aim to get comments to you tomorrow.

Thanks for responding to the legal comment responses; I'm currently checking with Carrie to see whether the response re the MCLG is sufficiently responsive to the comment as drafted – or whether we need to address it more specifically (she was the one who had initially flagged this one as requiring a response).

Pooja

Pooja S. Parikh
Attorney- Advisor

U.S. Environmental Protection Agency
Office of General Counsel, Water Law Office
Phone: 202 564-0839
Email: parikh.pooja@epa.gov

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Wednesday, March 11, 2020 9:22 AM
To: Parikh, Pooja <Parikh.Pooja@epa.gov>
Subject: RE: Request for OGC Review - Court Filing Perchlorate Communications Plan

Hi Pooja,

Please let me know if you also have any feedback for me on the Economic Assessment Responses to comments that I sent you last week.

Also attached you can see my response to some of the comments that you and Carrie had for me. I wanted to point out that I think there is a strategy that we should consider regarding avoiding a controversy over defining the health effect level outside of the MCLG constrains. Let me know if you would like to talk about this.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Parikh, Pooja <Parikh.Pooja@epa.gov>
Sent: Tuesday, March 10, 2020 4:05 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: Request for OGC Review - Court Filing Perchlorate Communications Plan

Ok, I expect I'll have time tomorrow to review.

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Tuesday, March 10, 2020 3:38 PM
To: Parikh, Pooja <Parikh.Pooja@epa.gov>
Subject: RE: Request for OGC Review - Court Filing Perchlorate Communications Plan

Hi Pooja,

I am not certain about timing, all I heard was that we needed to have this ready for when the filing takes place. I will get back to you soon about this.

Thanks
Sam
==========

Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Parikh, Pooja <Parikh.Pooja@epa.gov>
Sent: Tuesday, March 10, 2020 3:03 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: Request for OGC Review - Court Filing Perchlorate Communications Plan

Thanks for sending this. Sorry, I haven't had a chance to review yet – but it is on my to-do. What is the timing on this?

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, March 09, 2020 2:15 PM
To: Parikh, Pooja <Parikh.Pooja@epa.gov>
Subject: Request for OGC Review - Court Filing Perchlorate Communications Plan

Hi Pooja,

I was asked by Eric Burneson to reach out to OGC to request your review of the attached draft communications plan that we have prepared in anticipation of the filing with the court regarding the withdrawal of the Reg Det for Perchlorate. We are requesting your review because this is associated with the court filing.

This document has been reviewed by Eric and once I get your feedback, I will forward the revised document to the Communications people and to OGWDW.

Thank You
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 11/8/2019 5:59:42 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: Revised Briefing Document
Attachments: Option Selection for Perchlorate 11-8-19 v1.docx

Hi Lisa,

Here is the revised document. The edits are highlighted. Let me know if you have any comments or edits.

Thanks
Sam

==========

Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 4/29/2020 5:42:55 AM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: Draft Perchlorate Response to Comment Document
Attachments: Consolidated Perchlorate Draft Comment Response Document 4-29-20.docx

Hi Lisa,

Attached is the draft Perchlorate RtC Document. I incorporated the final input provided by ORD. This version also includes annotated comments from reviewers. Let me know if we should also provide a clean copy for review at this stage.

Thanks
Sam

==========

Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 2/21/2020 3:15:18 PM
To: McLain, Jennifer L. [McLain.Jennifer@epa.gov]
CC: Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]; Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]; Tiago, Joseph [Tiago.Joseph@epa.gov]; Wadlington, Christina [Wadlington.Christina@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Revised Document
Attachments: Perchlorate Reduction Outreach Plan v2.docx; Perchlorate Reductions 2-19-20 v1.docx; Perchlorate Recommendations for PWS 2-21-20.docx

Jennifer: We have updated the recommendations document to reflect the comments you provided earlier. Attached also is a plan to contact States and AWWA next week to verify our information and discuss with the states what assistance might be provided.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: Burneson, Eric
Sent: Thursday, February 20, 2020 4:19 PM
To: McLain, Jennifer L. <Mclain.Jennifer@epa.gov>
Cc: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Christ, Lisa (Christ.Lisa@epa.gov) <Christ.Lisa@epa.gov>
Subject: RE: Revised Document

Jennifer;
Attached please find revised perchlorate documents. We have revised the perchlorate reductions document with a view towards public release. We have also prepared the attached plan to work next week with ASDWA and AWWA to verify information about the systems and prepare states to assist systems.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: McLain, Jennifer L.
Sent: Wednesday, February 12, 2020 11:24 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>

Cc: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>
Subject: RE: Revised Document

Eric – would you please review this document with an eye towards the future public version. Once you have a chance to talk to the team, I would appreciate a plan for stakeholder engagement/outreach.

Thanks
Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Wednesday, February 12, 2020 9:53 AM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Subject: FW: Revised Document

Attached is the update on systems and perchlorate reductions. The only outstanding system is in LA.

From: Christ, Lisa
Sent: Wednesday, February 12, 2020 9:50 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: FW: Revised Document

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, February 10, 2020 12:37 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Revised Document

Hi Lisa,

We got new information from the MD system. There was some misunderstanding with the information request but here is the latest.

The treatment plant at chapel hill was recently taken off line and it was replaced with new productions wells and treatment plant which started operations in January 27, 2020. Please see the new language that I have incorporated in the revised document below.

"EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that the Chapel Hill WFP was taken off line and it was replaced with a new treatment plant and five new production wells. The new treatment plant started operations on January 27, 2020. System personnel also indicated that monitoring was conducted in November 2019 and the analysis shows that perchlorate was not detected in either the source well water or the finished water."

Thanks
Sam
==========

Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Monday, February 10, 2020 10:31 AM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Revised Document

Thanks Sam.
Do we know exactly what the contractor asked each PWS? Based on this response: **EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that no follow-up/updated monitoring data for perchlorate is available.** It appears we only asked about monitoring…did the contractor ask about any changes in source water and/or treatment too?

Thanks,
Lisa

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, February 10, 2020 8:14 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: Revised Document

Hi Lisa,

We heard back from the Chapel Hill system in MD and they do not have new data for Perchlorate. The document has been updated accordingly. Please see attached.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 5/19/2020 6:05:32 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: Draft Perchlorate Response to Comment Document
Attachments: Consolidated Perchlorate Draft Comment Response Document 5-19-20 v1 Clean.docx; Consolidated Perchlorate Draft Comment Response Document 5-19-20 v1 Redline.docx

Hi Lisa,

Attached are the redline and clean versions of the draft Perchlorate RtC Document. These incorporate all the suggested edits we have received so far from Eric, OGC, Team Members and others.

Let me know if you have any questions.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 1/17/2020 4:43:37 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
CC: Khera, Rajiv [Khera.Rajiv@epa.gov]
Subject: Supplemental Information - Perchlorate
Attachments: Supplemental Info - Perchlorate Option Selection 1-17-20 v1.docx

Hi Lisa,

Here is the document which provides the supplemental information requested about Perchlorate. I incorporated relevant input which was provided by staff from OLEM and OPP. Let me know if you have any questions or suggested edits.

Thanks
Sam

==========

Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 12/2/2019 9:35:35 PM
To: Mclain, Jennifer [Mclain.Jennifer@epa.gov]
CC: Tiago, Joseph [Tiago.Joseph@epa.gov]; Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: Perchlorate Briefing Document
Attachments: Redline-Responses - Option Selection for Perchlorate 11-21-19 v1 jlmkw.docx; Clean Version - Option Selection for Perchlorate 12-2-19 v1.docx

Jennifer
Attached are a clean and redline copy of the perchlorate briefing document with your edits incorporated and your comments/questions addressed. If you are comfortable with the attached I recommend you transmit the clean version to OW and that we bring a copy to OLEM for our discussion tomorrow.

Eric

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 5/19/2020 2:35:29 PM
To: McLain, Jennifer L. [McLain.Jennifer@epa.gov]
CC: Tiago, Joseph [Tiago.Joseph@epa.gov]; Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]
Subject: RE: Notice of Final Action on Perchlorate
Attachments: Perchlorate Action Memo 5-19-20.docx; Draft Perchlorate Final Action FRN 5-19-20 v1.docx; Transmittal Memo JM to DR 5-18-20.docx

Attached is a clean version of the notice with your edits accepted. Also attached is a clean version of the Action memo with the edits I sent you last night accepted. Lastly attached is the unchanged memo from you to Dave Ross.

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Tuesday, May 19, 2020 9:15 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Eric – I have made two minor edits in the attached. I will send this to Charlotte so that she can see how we've addressed her comments. At the same time we will submit formally to OW. Please send us the final clean versions of the memos and the action for that process.

Thanks much
Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, May 18, 2020 8:42 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Jennifer:
I don't believe a discussion is necessary. Edits and responses to the questions are in the attached. Please let us know if a revised clean version is needed.
Eric

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Monday, May 18, 2020 5:34 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: FW: Notice of Final Action on Perchlorate

Eric – please let me know if you want to discuss.

From: Bertrand, Charlotte <Bertrand.Charlotte@epa.gov>
Sent: Monday, May 18, 2020 5:29 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Braschayko, Kelley <braschayko.kelley@epa.gov>; Tiago, Joseph

<Tiago.Joseph@epa.gov>; Aguirre, Janita <Aguirre.Janita@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Thanks – couple of bubble box questions and then I had one redline edit I added to the Notice.

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Monday, May 18, 2020 3:01 PM
To: Bertrand, Charlotte <Bertrand.Charlotte@epa.gov>
Cc: Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Braschayko, Kelley <braschayko.kelley@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Aguirre, Janita <Aguirre.Janita@epa.gov>
Subject: FW: Notice of Final Action on Perchlorate

Charlotte – as agreed, I'm sending you the draft final perchlorate FRN for review. The redline includes the changes made since the FAR. I'm also including the draft Action Memo. Please let us know if your preference is to have these submitted to OW through CMS now or after you have reviewed. Let me know if you want to talk.

Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, May 18, 2020 2:48 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FW: Notice of Final Action on Perchlorate

Jennifer:

Attached for transmission to OW are revised versions of the FRN for the Perchlorate Final Action. There is both a clean and track changes version that includes edits made since initiating FAR (including the edits you asked for on Saturday and adding 3 more SAB recommendations to page 14 that were in the proposal but were not included in the draft we provided you on Friday). Also please find clean version of the transmittal memo from you to Dave Ross and the Action memo incorporating your edits.

Please note that there is also a redline version of the Action Memo for you to see the responses to your comments on the document. I do not recommend transmitting that memo to OW.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, May 18, 2020 2:18 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Hi Eric,

Attached are the revised Redline and Clean versions of the Perchlorate FR Notice. Once we are ready for OP's submittal to OMB let me know and I will provide a version that adheres to OP's file name formatting guidelines.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, May 18, 2020 1:14 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Sam

1. Change the title please. This was requested by OGC at Sr. Leadership levels.
2. Provide the same level of detail on the SAB recommendations as was included in the proposal.
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From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, May 18, 2020 12:41 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

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1- Page #1, Notice Tittle: We did not accept the edits to the notice tittle. Because, the tittle of the notice was specifically crafted by OGC to capture the multiple actions EPA is taking. Suggest consulting with OGC before modifying this tittle.
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3- Page #26, Missing HRRCA Text: This language was offered by TAB in its 5-13-20 version of the draft FRN, but it did not show up in the version provided by OGWDW with Eric's & Jennifer's comments. We have inserted the language here for the reviewer's consideration. Please advise if we should keep it.

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Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, May 18, 2020 8:42 AM
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Cc: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: FW: Notice of Final Action on Perchlorate

Lisa and Sam
Attached are Jennifer's comments and edits on the draft FRN. I have responded to her questions in the attached and made some additional edits. Can you please get a revised clean version and another redline version that compares this document and the version that was distributed to FAR?
Thanks for your work on this.
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From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Saturday, May 16, 2020 11:39 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Looks very good. See p. 6 for my only concern w/the revisions.

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Sent: Friday, May 15, 2020 5:03 PM
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Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: Notice of Final Action on Perchlorate

Jennifer

Attached for your approval and transmittal to the Office of Water for their approval and transmittal to the Office Policy for initiation of interagency review is a *Federal Register* notice titled: "Notice of Final Action on Perchlorate." Also attached for your review are a draft transmittal memo from you to the Assistant Administrator of Water, a draft Action Memorandum and a track changes version of the FR notice that denotes the changes made as a result of Final Agency Review.

On February 11, 2011, the EPA published a determination to regulate perchlorate in drinking water (76 FR 7762). On June 26, 2019 (84 FR 30524), the EPA published the proposed National Primary Drinking Water Regulation for Perchlorate and requested public comments on multiple alternative actions, including withdrawing the 2011 determination to regulate perchlorate. The EPA received approximately 1,500 comments on the proposed rule. In the attached notice, the EPA is withdrawing the 2011 Regulatory

Determination and is making a final determination not to regulate perchlorate based on the Agency's consideration of public comments and the best available information.

I recommend that you approve and transmit the attached notice to the Office of Water for their review, approval and transmission to the Office of Policy to initiate interagency review in accordance with Executive Order 12866. If you need additional information or have questions pertaining to any aspect of this notice, please call me or have your staff contact Samuel Hernandez at 202-564-1735.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 11/15/2019 7:32:13 PM
To: Albert, Ryan [Albert.Ryan@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Revised briefing document - Perchlorate
Attachments: Option Selection for Perchlorate 11-15-19 v1.docx

Ex. 5 Deliberative Process (DP)

From: Burneson, Eric
Sent: Friday, November 15, 2019 2:15 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Christ, Lisa (Christ.Lisa@epa.gov) <Christ.Lisa@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>; Albert, Ryan <Albert.Ryan@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Wehling, Carrie <Wehling.Carrie@epa.gov>; Wendelowski, Karyn <wendelowski.karyn@epa.gov>; Behl, Betsy <Behl.Betsy@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Weisman, Richard <Weisman.Richard@epa.gov>
Subject: RE: Revised briefing document - Perchlorate

Sam:
Thank you for preparing a revised briefing to respond to the input received in our prebrief. I have made additional edits to address requests received from OW leadership. I have left sections highlighted where OGC input is still needed. I also

Ex. 5 Deliberative Process (DP)

We will not be briefing the Administrator for the next several weeks but we do have an opportunity for OW review of the document so lets try to have revisions next week.
Please include OST on the next version. I have copied Betsy on the attached so that she can see the latest but you should also share with Greg and Jamie.

Eric

From: Hernandez-Quinones, Samuel
Sent: Wednesday, November 13, 2019 12:32 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: Revised briefing document - Perchlorate

Hi Eric,

Attached is a revised version of the briefing document, based on Jennifer's direction and comments during last week's meeting. Lisa reviewed this version and provided additional edits. I left two placeholders in this document for the input from OLEM as well as from OGC.

I sent this draft version to Karyn and she is working on providing OGC's input to us. Let me know if you have comments or any suggested edits.

Thanks
Sam
==========

Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 12/2/2019 3:38:00 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
CC: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Khera, Rajiv [Khera.Rajiv@epa.gov]
Subject: FW: Perchlorate
Attachments: Option Selection for Perchlorate 11-21-19 v1 jlmkw.docx

Lisa:
Can you review the attached briefing with Jennifer and Karyn's edits to confirm we are comfortable edits and have addressed the questions.
Please note that Betsy Behl stated she is comfortable and I have contacted OLEM about scheduling the meeting.

Eric

From: Wendelowski, Karyn
Sent: Wednesday, November 27, 2019 10:51 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Wehling, Carrie <Wehling.Carrie@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Behl, Betsy <Behl.Betsy@epa.gov>
Subject: Re: Perchlorate

Hi Eric - attached are a few edits and responses to Jennifer's questions. I've also let DOJ know the decision is now likely to occur mid-December.

Karyn

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Tuesday, November 26, 2019 4:24 PM
To: Wendelowski, Karyn <wendelowski.karyn@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Wehling, Carrie <Wehling.Carrie@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Behl, Betsy <Behl.Betsy@epa.gov>
Subject: RE: Perchlorate

Karyn:
The briefing has not happened nor is it scheduled. I have asked the team to assume that we will not brief the Administrator until mid December based upon input from OW – IO. Attached is a revised briefing from Jennifer McLain.

If you are in tomorrow it would be good to get your input on a few questions related to this briefing. Thanks

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: Wendelowski, Karyn
Sent: Tuesday, November 26, 2019 1:33 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>; Albert, Ryan <Albert.Ryan@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Wehling, Carrie <Wehling.Carrie@epa.gov>; Behl, Betsy <Behl.Betsy@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Weisman, Richard <Weisman.Richard@epa.gov>
Subject: Perchlorate

Hi All: - DOJ has asked me to check in with you on where we are with respect to schedule and timing. Has a briefing occurred? Any decisions?

Thanks (and Happy Thanksgiving),

Karyn

Karyn Wendelowski
Attorney-Advisor
Water Law Office
Office of General Counsel
(202)564-5493

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 10/30/2019 7:18:06 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: perchlorate draft OS brief
Attachments: Options Selection for Perchlorate V1 10-30-19.docx

Hi Lisa,

Here is a revised version of the document.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Wednesday, October 30, 2019 11:02 AM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: perchlorate draft OS brief

Hi Sam,
Attached is the draft briefing document we discussed. Please add, revised, deleted, etc.

Lisa

Lisa Christ
Chief, Targeting and Analysis Branch
Office of Ground Water and Drinking Water
202-564-8354

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 1/15/2020 3:16:10 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Perchlorate Team Meeting
Attachments: Draft Perchlorate Compendium.docx

FYI.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Hernandez-Quinones, Samuel
Sent: Monday, December 09, 2019 11:02 AM
To: Miller, Gregory <Miller.Gregory@epa.gov>
Subject: RE: Perchlorate Team Meeting

Ok, we can have a call later in the week.

Also, I am attaching here a copy of the draft compendium of comments for Perchlorate. I think you will be interested in seeing the comments on section 8.1. Let me know if you have any questions.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

-----Original Appointment-----
From: Miller, Gregory <Miller.Gregory@epa.gov>
Sent: Monday, December 09, 2019 7:28 AM
To: Hernandez-Quinones, Samuel
Subject: Tentative: Perchlorate Team Meeting
When: Wednesday, December 11, 2019 2:00 PM-2:45 PM (UTC-05:00) Eastern Time (US & Canada).
Where: DCRoomEast2406/DC-ICC-OW-OGWDW

Hi Sam,
I'm not going to be available for this meeting. I'll give you a call to check in. Thanks.

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 3/3/2020 9:36:59 PM
To: McLain, Jennifer L. [McLain.Jennifer@epa.gov]
CC: Tiago, Joseph [Tiago.Joseph@epa.gov]; Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Materials for tomorrow's Briefing: Perchlorate
Attachments: Decision for Perchlorate Final Regulatory Action_2_26_20.docx; Option Selection for Perchlorate_final_01.09.2020.pdf

Jennifer: Attached are the materials that we would add to the recommendations and reductions documents (that were transmitted to OW) for a discussion with the Administrator. We note that the schedules in the briefing we gave the Administrator on 1/9/20 are now out of date. Below is an update for the withdrawal schedule that assumes a meeting occurs on March 16.

Perchlorate Schedule - Draft 2/24/2020			
Activity	**start**	**end**	**No. Days**
Option selection AA	1/7/2020	1/7/2020	0
Options selection Administrator	1/9/2020	1/9/2020	0
Prepare additional support documents	1/10/2020	1/24/2020	14
Brief Administrator	3/16/2020	3/20/2020	5
OW Prepares Final Regulatory Determination Package (FRN, comment response document etc.)	1/25/2020	4/4/2020	70
Final Agency Review	4/5/2020	4/26/2020	21
OMB briefing & ROCIS Submission	4/27/2020	5/4/2020	7
EO12866 review	5/5/2020	6/11/2020	37
Final Signature and Rollout	6/12/2020	6/19/2020	7
Consent Decree Signature Deadline		**6/19/2020**	

Ex. 5 Deliberative Process (DP)

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 5/18/2020 6:47:55 PM
To: McLain, Jennifer L. [McLain.Jennifer@epa.gov]
CC: Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]; Tiago, Joseph [Tiago.Joseph@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: FW: Notice of Final Action on Perchlorate
Attachments: Draft Perchlorate Final Action FRN 5-18-20 v1 Redline.docx; Draft Perchlorate Final Action FRN 5-18-20 v1 Clean.docx; Perchlorate Action Memo 5-18-20.docx; Perchlorate Action Memo 5-18-20redline.docx; Transmittal Memo JM to DR 5-18-20.docx

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Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

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202-564-1735

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<Guilaran.Yu-Ting@epa.gov>
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I recommend that you approve and transmit the attached notice to the Office of Water for their review, approval and transmission to the Office of Policy to initiate interagency review in accordance with Executive Order 12866. If you need additional information or have questions pertaining to any aspect of this notice, please call me or have your staff contact Samuel Hernandez at 202-564-1735.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 2/26/2020 1:21:05 PM
To: McLain, Jennifer L. [McLain.Jennifer@epa.gov]
CC: Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]; Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]; Tiago, Joseph [Tiago.Joseph@epa.gov]; Wadlington, Christina [Wadlington.Christina@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Revised Document
Attachments: Perchlorate Reductions 2-25-20 v1.docx; Perchlorate Recommendations for PWS 2-25-20 v1.docx

Jennifer: Attached please find clean copies of the recommendations and reductions documents for perchlorate. We have incorporated your edits. Please note with respect to your question about CCR reporting of perchlorate monitoring

CCR regulations under 141.153.(d)(1) requires the CCR include data on detected contaminants subject to mandatory monitoring including

i. Contaminants subject to an MCL, action level, MRDL or TT
ii. Contaminants for which monitoring is required under the UCMR
iii. Disinfection byproducts or micriobial contaminants for which monitoring is required.

Ex. 5 Deliberative Process (DP)

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: McLain, Jennifer L.
Sent: Sunday, February 23, 2020 9:13 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: Revised Document

Thank you Eric & Lisa – The attached contain a very few edits/comments. And then, these are ready to go to OW for review. Regarding the outreach plan, continue to pursue the discussions with ASDWA and AWWA as we discussed and agreed to with Dave. However, I'm not sure that we can say these reports will be released soon, maybe it is better to say that there is the potential for them to be issued in the near term.

Thanks much,
Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Friday, February 21, 2020 10:15 AM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Subject: FW: Revised Document

Jennifer: We have updated the recommendations document to reflect the comments you provided earlier. Attached also is a plan to contact States and AWWA next week to verify our information and discuss with the states what assistance might be provided.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: Burneson, Eric
Sent: Thursday, February 20, 2020 4:19 PM
To: McLain, Jennifer L. <Mclain.Jennifer@epa.gov>
Cc: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Christ, Lisa (Christ.Lisa@epa.gov) <Christ.Lisa@epa.gov>
Subject: RE: Revised Document

Jennifer;
Attached please find revised perchlorate documents. We have revised the perchlorate reductions document with a view towards public release. We have also prepared the attached plan to work next week with ASDWA and AWWA to verify information about the systems and prepare states to assist systems.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: McLain, Jennifer L.
Sent: Wednesday, February 12, 2020 11:24 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>
Subject: RE: Revised Document

Eric – would you please review this document with an eye towards the future public version. Once you have a chance to talk to the team, I would appreciate a plan for stakeholder engagement/outreach.

Thanks
Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Wednesday, February 12, 2020 9:53 AM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Subject: FW: Revised Document

Attached is the update on systems and perchlorate reductions. The only outstanding system is in LA.

From: Christ, Lisa
Sent: Wednesday, February 12, 2020 9:50 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: FW: Revised Document

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, February 10, 2020 12:37 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Revised Document

Hi Lisa,

We got new information from the MD system. There was some misunderstanding with the information request but here is the latest.

The treatment plant at chapel hill was recently taken off line and it was replaced with new productions wells and treatment plant which started operations in January 27, 2020. Please see the new language that I have incorporated in the revised document below.

"EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that the Chapel Hill WFP was taken off line and it was replaced with a new treatment plant and five new production wells. The new treatment plant started operations on January 27, 2020. System personnel also indicated that monitoring was conducted in November 2019 and the analysis shows that perchlorate was not detected in either the source well water or the finished water."

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW

Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Monday, February 10, 2020 10:31 AM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Revised Document

Thanks Sam.
Do we know exactly what the contractor asked each PWS? Based on this response: **EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that no follow-up/updated monitoring data for perchlorate is available.** It appears we only asked about monitoring…did the contractor ask about any changes in source water and/or treatment too?

Thanks,
Lisa

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, February 10, 2020 8:14 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: Revised Document

Hi Lisa,

We heard back from the Chapel Hill system in MD and they do not have new data for Perchlorate. The document has been updated accordingly. Please see attached.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 11/14/2019 8:51:37 PM
To: Huff, Lisa [Huff.Lisa@epa.gov]
CC: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: Perchlorate briefing
Attachments: Option Selection for Perchlorate 11-12-19 v1.docx

Hi Lisa,

I sent a revised draft version of the briefing document to Eric earlier this week. We are waiting for additional input that OGC will provide to us. Here is the revised document, as reviewed by Lisa, that I shared with Eric. If you have additional information, I will be glad to incorporate into the document.

I will be in the office tomorrow morning if you want to hand those notes to me, or you can also email them.

Thanks
Sam

==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

-----Original Message-----
From: Huff, Lisa <Huff.Lisa@epa.gov>
Sent: Thursday, November 14, 2019 3:37 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: Perchlorate briefing

Sam,
I just had a conversation with Eric. He said the meeting with with Dave Ross and the Administrator has been delayed however he said we need to put together the briefing materials ASAP. He gave me a brief summary of the 3 options to reflect based on direction from last week. I can email you those point but thought you might have in your notes. He had one addition that is for the option recommending a MCL we should specify that value would be 18. Have you been working on preparing materials? Eric was hoping to have them by tomorrow for his review. Please let me know. I'm out of the office for an appt. but will follow up via email shortly.

Lisa

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 4/24/2020 1:09:36 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: Response to comment document
Attachments: Draft Responses Section 8 - Health Effects 4-24-20 v1.docx; Consolidated Perchlorate Draft Comment Response Report 4-24-20 v1.docx

Hi Lisa,

Attached you will find the consolidated response to comment document. To make the review process easier in this stage, I decided to have a separate file that includes only Section 8 (Health Effects). I think it is easier this way because it is the largest section in the document and providing edits and comments on the lager document might impact the editorial format on other sections.

I have only received partial input from ORD, I told Lynn that I could not wait any longer for their input and that I would send the document forward for review and that I was leaving placeholders for their input. There are only a handful of comments pending. She is aware of our very aggressive schedule on perchlorate.

I will be working in the coming days with the team to make another QA of the document to make sure that any issues we find are captured in the next round of revisions. I am also working on the cover and front matter of the report.

Thank You
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 9/12/2019 4:10:34 PM
To: Mclain, Jennifer [Mclain.Jennifer@epa.gov]; Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]
CC: Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Tiago, Joseph [Tiago.Joseph@epa.gov]
Subject: Perchlorate comment summary
Attachments: Perchlorate Comment Summary V4.docx

Jennifer and Yu Ting:
Attached please find a summary of the comments on the proposed perchlorate drinking water regulation. This issue came up in the hearing prep meeting for the Administrator yesterday and I would like to present the attached in the OW biweekly tomorrow. Please let me know if you have any comments or concerns with the attached.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 9/12/2019 12:46:20 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: draft summary of perchlorate public comments -- Eric was wondering when this would be ready?
Attachments: Perchlorate Comment Summary V4.docx

Hi Lisa,

Here is the revised summary document. It now accounts for all the comments uploaded in the docket.

Thanks
Sam

==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Wednesday, September 11, 2019 4:18 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FW: draft summary of perchlorate public comments -- Eric was wondering when this would be ready?
Importance: High

From: Christ, Lisa
Sent: Wednesday, September 11, 2019 12:02 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FW: draft summary of perchlorate public comments

Hi Sam,
Please see Eric's request below. I think he'd like to share with OW on Friday.

Thanks,
Lisa

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Wednesday, September 11, 2019 12:00 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: draft summary of perchlorate public comments

Thanks Lisa this breakdown is helpful but it pointed out to me that the 109 extensive and substantive letters don't all appear to be summarized.

I think there isn't a need to organize the commenters by organization type and there are some groups that are hard to categorize (i.e. we have ACWA as a regulated stakeholder but AWWA is a trade organization when the both represent drinking water utilities) I also think there is redundancy in the summary of the comments that I tried to eliminate in the attached.
Can the team take a look and see if there are organizations that have submitted extensive and substantive comments that we have not listed and if so please list them in the categories of support that are in the attached.

From: Christ, Lisa
Sent: Wednesday, September 11, 2019 7:46 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: FW: draft summary of perchlorate public comments

Revised

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Tuesday, September 10, 2019 4:04 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: draft summary of perchlorate public comments

Hi Lisa,

Here is a revised version which incorporates previously suggested edits.

- We received 6 comment letters in support of the proposed rule at 56 ppb.
- I cannot categorically confirm that the mass mailing campaign was organized by any group, so I am removing that designation from the summary document.
- From the individual substantive letters
    - 1 supports withdrawal option
    - 1 supports 90 ppb option
    - 6 support 18 ppb option
    - 23 support regulation at a stricter level than 18pbb

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Tuesday, September 10, 2019 1:44 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FW: draft summary of perchlorate public comments

Hi Sam,
As follow up can you please:

- Confirm we did not get support for regulation at 56 ppb
- Confirm if NRDC is mentioned as the originator of the mass campaign

- Count the 88 individual comments that 1- support withdrawal, 2- support regulation (at any concentration).

Let me know if you have questions
Thanks,
Lisa

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Tuesday, September 10, 2019 1:30 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>; Lombardi, Thomas <lombardi.thomas@epa.gov>; Alattar, Zaineb <alattar.zaineb@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: RE: draft summary of perchlorate public comments

Also There are three categories of commenters presented

1. Support withdrawal
2. Support a stricter than proposed standard
3. Neutral

Does this mean there were no commenters in support of the proposed MCLG/MCL?

From: Burneson, Eric
Sent: Tuesday, September 10, 2019 1:27 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>; Lombardi, Thomas <lombardi.thomas@epa.gov>; Alattar, Zaineb <alattar.zaineb@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: RE: draft summary of perchlorate public comments

Thanks Lisa: My only comment is that unless the comment campaign letters clearly state they are submitting comments organized by NRDC or there is public information from NRDC clearly stating that they organized a comment campaign we should not attribute the campaign to them.
Eric

From: Christ, Lisa
Sent: Tuesday, September 10, 2019 12:27 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>; Lombardi, Thomas <lombardi.thomas@epa.gov>; Alattar, Zaineb <alattar.zaineb@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: draft summary of perchlorate public comments

Eric,
Attached is a high level summary of the public comments received on the perchlorate proposal. OGC requested a summary to prepare the notice to the court requesting an extension of the consent decree final rule deadline. Let me know if you have questions or would like to discuss.
Lisa

Lisa Christ
Chief, Targeting and Analysis Branch
Office of Ground Water and Drinking Water

202-564-8354

Message

From: Khera, Rajiv [Khera.Rajiv@epa.gov]
Sent: 2/25/2020 8:28:14 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
CC: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: Draft Perchlorate Compendium HRRCA sections 8-1 to 8-4 rk
Attachments: Draft Perchlorate Compendium HRRCA sections 8-1 to 8-4 rk.docx

Hi Sam-The attached has responses to all HRRCA and Treatment comments (sections 8.3 and 8.4) including a general response for the entire HRRCA section (start of 8.3) and responses to a few additional non-HRRCA sections (see comments 8.1 and 9.13). Part of some of our responses need to be cross referenced to other responses that are being developed by other team members, so for now those parts have been highlighted. Let me know if you have any questions. Thanks
Rajiv

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 9/10/2019 8:03:47 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: draft summary of perchlorate public comments
Attachments: Perchlorate Comment Summary V2.docx

Hi Lisa,

Here is a revised version which incorporates previously suggested edits.

- We received 6 comment letters in support of the proposed rule at 56 ppb.
- I cannot categorically confirm that the mass mailing campaign was organized by any group, so I am removing that designation from the summary document.
- From the individual substantive letters
  - 1 supports withdrawal option
  - 1 supports 90 ppb option
  - 6 support 18 ppb option
  - 23 support regulation at a stricter level than 18pbb

Thanks
Sam

==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Tuesday, September 10, 2019 1:44 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FW: draft summary of perchlorate public comments

Hi Sam,
As follow up can you please:

- Confirm we did not get support for regulation at 56 ppb
- Confirm if NRDC is mentioned as the originator of the mass campaign
- Count the 88 individual comments that 1- support withdrawal, 2- support regulation (at any concentration).

Let me know if you have questions
Thanks,
Lisa

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Tuesday, September 10, 2019 1:30 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Newcamp,

Caitlin <Newcamp.Caitlin@epa.gov>; Lombardi, Thomas <lombardi.thomas@epa.gov>; Alattar, Zaineb <alattar.zaineb@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: RE: draft summary of perchlorate public comments

Also There are three categories of commenters presented

1. Support withdrawal
2. Support a stricter than proposed standard
3. Neutral

Does this mean there were no commenters in support of the proposed MCLG/MCL?

From: Burneson, Eric
Sent: Tuesday, September 10, 2019 1:27 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>; Lombardi, Thomas <lombardi.thomas@epa.gov>; Alattar, Zaineb <alattar.zaineb@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: RE: draft summary of perchlorate public comments

Thanks Lisa: My only comment is that unless the comment campaign letters clearly state they are submitting comments organized by NRDC or there is public information from NRDC clearly stating that they organized a comment campaign we should not attribute the campaign to them.
Eric

From: Christ, Lisa
Sent: Tuesday, September 10, 2019 12:27 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>; Lombardi, Thomas <lombardi.thomas@epa.gov>; Alattar, Zaineb <alattar.zaineb@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: draft summary of perchlorate public comments

Eric,
Attached is a high level summary of the public comments received on the perchlorate proposal. OGC requested a summary to prepare the notice to the court requesting an extension of the consent decree final rule deadline. Let me know if you have questions or would like to discuss.
Lisa

Lisa Christ
Chief, Targeting and Analysis Branch
Office of Ground Water and Drinking Water
202-564-8354

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 5/15/2020 9:03:15 PM
To: McLain, Jennifer L. [McLain.Jennifer@epa.gov]
CC: Christ, Lisa [Christ.Lisa@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Tiago, Joseph [Tiago.Joseph@epa.gov]; Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]
Subject: Notice of Final Action on Perchlorate
Attachments: Draft Perchlorate Final Action FR Notice 5-15-20 v1 Redline (002).docx; Draft Perchlorate Final Action FR Notice 5-15-20 v1.docx; Perchlorate Action Memo 5-15-20.docx; Transmittal Memo JM to DR 5-15-20.docx

Jennifer

Attached for your approval and transmittal to the Office of Water for their approval and transmittal to the Office Policy for initiation of interagency review is a *Federal Register* notice titled: "Notice of Final Action on Perchlorate." Also attached for your review are a draft transmittal memo from you to the Assistant Administrator of Water, a draft Action Memorandum and a track changes version of the FR notice that denotes the changes made as a result of Final Agency Review.

On February 11, 2011, the EPA published a determination to regulate perchlorate in drinking water (76 FR 7762). On June 26, 2019 (84 FR 30524), the EPA published the proposed National Primary Drinking Water Regulation for Perchlorate and requested public comments on multiple alternative actions, including withdrawing the 2011 determination to regulate perchlorate. The EPA received approximately 1,500 comments on the proposed rule. In the attached notice, the EPA is withdrawing the 2011 Regulatory Determination and is making a final determination not to regulate perchlorate based on the Agency's consideration of public comments and the best available information.

I recommend that you approve and transmit the attached notice to the Office of Water for their review, approval and transmission to the Office of Policy to initiate interagency review in accordance with Executive Order 12866. If you need additional information or have questions pertaining to any aspect of this notice, please call me or have your staff contact Samuel Hernandez at 202-564-1735.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 1/7/2020 8:22:31 PM
To: Mclain, Jennifer [Mclain.Jennifer@epa.gov]; Wehling, Carrie [Wehling.Carrie@epa.gov]
CC: Wendelowski, Karyn [wendelowski.karyn@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Khera, Rajiv [Khera.Rajiv@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Huff, Lisa [Huff.Lisa@epa.gov]; Tiago, Joseph [Tiago.Joseph@epa.gov]; Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]
Subject: Revised Perchlorate Briefing
Attachments: Option Selection for Perchlorate 1-9-20v1.docx

Jennifer and Carrie:
Attached for your review and comment is a revised Perchlorate Option Selection briefing that reflects the direction I heard in the discussion today including;

Ex. 5 Deliberative Process (DP)

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 1/28/2020 10:31:39 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: FOR REVIEW: Perchlorate Reductions
Attachments: Redline - Reductions of Perchlorate in Drinking Water 1-28-20 v1.docx

Hi Lisa,

Here is the revised version. Let me know if you have any comments or if you would like to discuss.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Tuesday, January 28, 2020 2:48 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FW: FOR REVIEW: Perchlorate Reductions
Importance: High

Sam – confirming you're addressing these?

From: McLain, Jennifer L. <Mclain.Jennifer@epa.gov>
Sent: Tuesday, January 28, 2020 2:33 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: RE: FOR REVIEW: Perchlorate Reductions

Lisa & team – My additional edits are attached. I will stop by to discuss later today.

Thanks
Jennifer

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Monday, January 27, 2020 11:23 AM
To: McLain, Jennifer L. <Mclain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Hernandez-Quinones, Samuel

<Hernandez.Samuel@epa.gov>
Subject: RE: FOR REVIEW: Perchlorate Reductions

Jennifer,
We have revised the draft document to address your edits/comments. There are a few places where we've replied in the comment bubbles. Let us know if you'd like to meet to discuss or if you have further edits/comments/questions.

Thank you,
Lisa

From: Mclain, Jennifer <Mclain.Jennifer@epa.gov>
Sent: Thursday, January 23, 2020 5:45 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: FOR REVIEW: Perchlorate Reductions

Thank you all for pulling this information together so quickly. The attached includes a number of comments, primarily around whether we have more information. I recognize that there are probably many instances where we just don't have anything else but I think there are a few places where we could find additional information. I'm happy to discuss.

Jennifer

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Wednesday, January 22, 2020 4:49 PM
To: Mclain, Jennifer <Mclain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: FOR REVIEW: Perchlorate Reductions

Jennifer,
Attached is the second document requested during option selection. There are 5 PWSs of the 15 we identified as having UCMR1 results >18ppb that have not responded to our request for updated information. They are highlighted in yellow. We will continue to try, but I wanted to get this to you sooner rather than later.
Let us know if you have questions, concerns or need additional information.
Lisa

From: Christ, Lisa
Sent: Wednesday, January 22, 2020 11:42 AM
To: Mclain, Jennifer <Mclain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FOR REVIEW: Perchlorate Recommendations for PWSs

Jennifer,
During option selection on 1/9 with Administrator Wheeler, he requested OGWDW prepare two documents:

1. Recommendations for PWSs that may be concerned about perchlorate in drinking water (attached)
2. Reductions in perchlorate levels and actions to reduce levels since UCMR1 (pending)

For your review is document #1, which incorporates edits from Eric and Christina. We are working on document #2 and should have a draft for your review soon.

Let us know if you have questions, concerns or need additional information.
Lisa

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 1/3/2020 6:03:12 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
CC: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Khera, Rajiv [Khera.Rajiv@epa.gov]; Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]
Subject: Perchlorate briefing
Attachments: Option Selection for Perchlorate 12-20-19v4.docx

Lisa:
I received comments from Jennifer on the perchlorate briefing and the attached reflects those comments. The most significant ask is to present the total population vs protected population breakdown as shown on page 4. Let me know if you have any concerns or if it is not possible to make the requested changes before noon on Monday. Thanks

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Khera, Rajiv [Khera.Rajiv@epa.gov]
Sent: 8/28/2019 6:43:20 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Post-closing docket update
Attachments: 0158.pdf; 0169.pdf; 0161.pdf; 0242.pdf; 0236.pdf; 0239.pdf; 0241.pdf; 0243.html; 0247.pdf; 0248.pdf; 0249.2.pdf; 0249.pdf; 0249.1.pdf

FYI

From: Geraldine Camilli <gcamilli@horsleywitten.com>
Sent: Tuesday, August 27, 2019 4:59 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>; Ashley Pasakarnis <apasakarnis@horsleywitten.com>
Subject: Post-closing docket update

Hi Sam,

Below is an update to the perchlorate docket with public comments posted as of this morning. Given that the docket closed yesterday, there will likely be more comments posted over the coming days, and we will keep you updated.

Of the 59 comments posted by the docket so far, the following were submitted by commenters other than the general public – copies of the letters are attached:

1. Salt River Pima-Maricopa Indian Community (SRPMIC) et al. (Doc. #0158)
2. Water Resources Department, Tohono O'odham Nation (Doc. #0161)
3. El Paso Water (Doc. #0169)
4. Massachusetts Department of Environmental Protection (MassDEP) (Doc. #0236)
5. Association of Metropolitan Agencies (AMWA) (Doc. #0239)
6. Metropolitan Water District of Southern California (Doc. #0241)
7. Division of Scientific Programs, California Office of Environmental Health Hazard Assessment (OEHHA) (Doc. #0242)
8. Innovative Water Care, LLC (Doc. #0243)
9. Environmental Protection Network (EPN) (Doc. #0247)
10. Association of State Drinking Water Administrators (ASDWA) (Doc. #0248)
11. Natural Resources Defense Council (NRDC) (Doc. #0249, and its two attachments 0249.1 and 0249.2)

We anticipate there will be at least once mass mailing campaign, but have not seen any officially posted by the docket yet.

In terms of numbers, please note that:

- The comment count on regulations.gov is 1,280, only 59 of which have been posted so far.
- As far as we can determine, the docket has "parked" about 1,400 letters for further evaluation, and we anticipate that most of those will be modified mass mailers.
- There are also another 20 or so pending various levels of docket review.
- Comment numbers at this time are in draft form (hence why they don't add up), but hopefully this gives you a better sense of what is coming.

Please let us know if you have any questions about the above, or would like additional information.
Kind regards,
Geraldine

Geraldine Camilli, P.E. | Project Manager – Environmental Engineer
Horsley Witten Group
90 Route 6A | Unit #1
Sandwich, MA 02563
Office: 508-833-6600
Cell: 617-642-7887

SALT RIVER

PIMA-MARICOPA INDIAN COMMUNITY

10005 East Osborn Road / Scottsdale, Arizona 85256

The Salt River Pima-Maricopa Indian Community's (SRPMIC or Community) Community Development Department's (CDD) Environmental Protection and Natural Resources (EPNR) Division in conjunction with the SRPMIC Office of the General Counsel (OGC) have reviewed the information on the proposed National Primary Drinking Water Regulation (NPDWR) for perchlorate in order to establish a Maximum Contaminant Level (MCL) and a health-based Maximum Contaminant Level Goal (MCLG) at 56 micrograms per liter. SRPMIC staff disagrees with the proposed 56 micrograms per liter and our comments and questions are below in regards to the three alternative regulatory options.

- An MCL and MCLG for perchlorate set at 18 micrograms per liter.

While an MCL of 18 micrograms per liter may be attainable for most Public Drinking Water Systems, it does not make that a safe number. If a recommendation must be made, then this number may be tentatively acceptable for now until additional, more thorough, scientific investigations are completed. There are numerous states that have already adopted lower limits (e.g. California 6 micrograms per liter MCL, and Iowa 4.9 micrograms per liter), and have done so while taking into consideration the multiple sources of perchlorate in which the public are exposed. The studies completed (according to EPA June 12, 2019 online PPT presentation "National Primary Drinking Water Regulation for Perchlorate: Proposed Rule" and Section III of the proposed rule document), arrive at the proposed numbers, but do not account for contaminated food (Jackson W.A., Joseph P., Laxman P., Tan K., Smith P.N., and Yu L., et al. Perchlorate accumulation in forage and edible vegetation. *J Agric Food Chem* 2005: 53: 369–373.), soil, air, and occupational exposure (unless it is unclear).

The Community questions whether the studies that EPA used to determine their proposed levels are accurate or sufficient enough to arrive at a "real, health-based" decision considering the disparity between the proposed numbers and some state numbers. Methodology and data from states with adopted levels should have been considered in EPA's decision, as should have studies on animals, and in people with thyroid problems.

Have there been any peer-reviewed, published studies on perchlorate using animals? If not, can resources be gathered from different sources (research institutions, federal agencies, etc.) to conduct these types of studies in order to

arrive at a more defensible "health-based" number? These tests would need to examine different exposure levels over time, and consider multiple age groups (not just based on interviews and surveys). Are studies currently being initiated on people with thyroid problems that reside in areas close to sources of perchlorate contamination? Can studies be done to follow the medical history of patients that, as of now, are found to have high levels of perchlorate in urine, in order to learn more about thyroid disruption, other possible health effects, and continuous long-term exposure, etc. (similar to "Perchlorate Exposure of the US Population, 2001-2002" from the Journal of Exposure Science and Environmental Epidemiology)? Can funds also be used to research the presence and effects of perchlorate in infants and children below the age of 6 years old? Did EPA look at the FDA's "Exploratory Survey Data on Perchlorate in Food 2004-2005" in its determination of a "health-based" level?

- An MCL and MCLG for perchlorate set at 56 or 90 micrograms per liter.

  A proposed MCL of 56 or 90 micrograms per liter has a large disparity from a number of state standards and proposed state standards (e.g. California, Massachusetts, Vermont, Maryland, and Arizona's Regional Screening Level). It would therefore be absurd to set an MCL and MCLG this high for perchlorate when states have already determined that their public water systems are able to clean to a safer level.

- Withdrawal of the Agency's 2011 determination to regulate perchlorate in drinking water, which was a reversal of the 2008 preliminary determination to not regulate perchlorate.

  Withdrawal of regulation will only encourage the industry to abandon any preventative measures to contain current contamination. Withdrawal will allow the industry to continue to manage their waste on a case by case basis.

  The Community, and similarly, other Tribal nations, rely on the EPA requirements and standards to support our efforts to keep Tribal waters safe from environmental health hazards. The agency's guidance/regulation may also help Tribal nations enforce possible contamination in the absence of existing local environmental rules and regulations (which could take some years to achieve). Native American communities already have a higher diabetes prevalence, according to "Traditions and Diabetes Prevention: A Healthy Path for Native Americans" from the American Diabetes Association. Having diabetes prevalence and possible exposure to perchlorate, which affects the thyroid, would only place the Community at a higher health disadvantage. Furthermore, Native American communities may not always have the resources to provide proper medical assistance, and already experience environmental injustice (equaling greater negative effects from contamination) based on where reservations are located. In conclusion, it is in the best interest of the Community and its members to expect and follow the most stringent and protective drinking water regulations in order to protect a health-wise vulnerable population.

Tohono O'odham Nation
Water Resources Department
PO Box 10
Sells, Arizona 85634
Phone: (520) 383-2362 Fax: (520) 383-5563

July 26, 2019

Samuel Hernandez
Office of Ground Water and Drinking Water
Standards and Risk Management Division
Environmental Protection Agency

These comments address the US Environmental Protection Agency (EPA) proposed National Primary Drinking Water Regulation for perchlorate to establish a Maximum Contaminant Level (MCL) and a health-based Maximum Contaminant Level Goal (MCLG) at 56 micrograms per liter (µg/l) (May 23, 2019). The current Interim Drinking Water Health Advisory level for perchlorate is 15 µg/l. The EPA refused to use all its scientific evidence that perchlorate (a neurotoxin) can affect neurodevelopment and intelligence quotient (IQ) in children[1]. This scientific information may have produced a proposed MCL and MCLG lower than 15 µg/l. The EPA's new proposed rule of 56 µg/l does not provide adequately protection to unborn children in the first trimester of pregnancy.

The EPA is seeking comments on three alternative regulatory options in its new proposed rule[2]:

1. An MCL and MCLG for perchlorate set at 18 micrograms per liter.
2. An MCL and MCLG for perchlorate set at 90 micrograms per liter.
3. Withdrawal of the agency's 2011 determination to regulate perchlorate in drinking water.

Prior to the new proposed rule of 56 µg/l, many environmental scientists believed that the EPA was moving towards protecting a mother's perchlorate exposure in the first trimester from fetal harm[3].

The EPA abruptly changed course by altering its decision in three significant ways[3]:

1. Rejecting five epidemiology studies showing harm at even lower exposure levels in favor of one IQ study [3,4].
2. Choosing an MCL that allows an IQ loss of 2 points even though the study showed a 1 point loss was statistically significant.
3. Dismissing an alternative, population-based method that the EPA (2017) once supported that reinforces the need for a more protective standard.

The Tohono O'odham Nation Water Resources Department (Department) believes that EPA's refusal to use all of its scientific evidence and its proposed MCL and MCLG of 56 µg/l lessens the Safe Drinking Water Act's ability to protect the public, especially the unborn and newborn, from adverse effects[3,5].

The Department believes the EPA is required to protect children from any harm to their brain development from perchlorate exposure during the first trimester; it is their duty and responsibility. The Department also believes the EPA's negligence in using one study to help deregulate parts of the Safe Drinking Water Act in favor of industry is not fair and reckless to the long term health of all Americans.

The true test for whether any MCL for perchlorate is safe will always be: If it was your wife and our unborn child being exposed, would you feel confident in giving them water with any amount of perchlorate.

The Department supports a perchlorate MCL and MCLG lower than the current 15 µg/l.

Respectfully yours,

Selso Villegas

Selso Villegas
Director, Water Resources Department
Tohono O'odham Nation

Literature Cited

1 Post-Meeting Peer Review Summary Report - External Peer Review for EPA's Proposed Approaches to Inform the Derivation of a Maximum Contaminant Level Goal for Perchlorate in Drinking Water. March 2018. 117p.

2 https://www.epa.gov/dwstandardsregulations/perchlorate-drinking-water

3 Neltner, Tom. EPA distorts the scientific evidence and fails to protect kids' brains in its proposed limit for perchlorate in drinking water. May 24, 2019.

4 https://www.thelancet.com/pdfs/journals/landia/PIIS2213-8587(15)00327-7.pdf

5 42 U.S.C §300g-1(b)(4)(A).

el paso WATER

August 2, 2019

The Honorable Andrew Wheeler
Administrator
Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

Dear Mr. Wheeler:

I want to thank you for the opportunity to comment on the Environmental Protection Agency's proposed rulemaking on perchlorate levels in drinking water. From our perspective, opportunities such as this are highly valuable in allowing public water utilities to contribute in a meaningful way to the development of sound policy that protects public drinking water resources.

Based on the EPA's chosen neurodevelopmental endpoints and the occurrence of perchlorate at the three given MCLs/MCLGs in drinking water systems, El Paso Water agrees with the EPA's determination that due to the low occurrence of perchlorate nationwide, this particular proposal does not present a meaningful opportunity for health risk reduction as is laid out in the Safe Drinking Water Act (SDWA).

In short, we believe this to be a solution in search of a problem. With national detection levels at less than two percent (and readings for the majority of tests were well below these thresholds), the frequency of occurrence is simply not sufficient to impose a regulatory burden on the vast majority of public water systems, including our own at El Paso Water.

In our own experience in El Paso, Texas, we have reviewed sampling records dating back to 2005. Of more than 750 samples for perchlorate, we had only one detection, which was at 17 micrograms per liter, far below the proposed regulatory levels. It was determined that this was naturally occurring perchlorate, yet because of this determination, additional sampling would be required across the system despite the single finding. While we currently have the in-house instrumentation to monitor for perchlorate, there is a cost attached for each time the sample goes through laboratory analysis, which is substantial at $25 per sample multiplied by 50 wells times the frequency of sampling

Even though our one reading was far below regulatory threshold, depending on the nature of the regulations put in place, Granular Activated Carbon (GAC) filtration might be required at the one well that produced the detection. At an estimated cost of $200,000 for the installation of a GAC filtration vessel, it may be more advantageous to abandon the well altogether.

EPWater also agrees with the EPA's statement on the cost-benefit analysis that, based on the parameters laid out by EPA and SDWA, the benefits do not justify the costs. We believe that our limited resources are better used elsewhere.

We support the EPA's efforts to continue periodic monitoring, research and modeling – especially in targeted areas with high detections of perchlorate to understand causes and provide guidance to states on any increasing levels that may warrant further evaluation of any public health impacts.

Sincerely,

John E. Balliew, P.E.
President & CEO
El Paso Water

Commonwealth of Massachusetts
Executive Office of Energy & Environmental Affairs

Department of Environmental Protection

One Winter Street Boston, MA 02108 • 617-292-5500

Charles D. Baker
Governor

Karyn E. Polito
Lieutenant Governor

Kathleen A. Theoharides
Secretary

Martin Suuberg
Commissioner

United States Environmental Protection Agency
Office of Water
1200 Pennsylvania Ave. NW
Washington DC 20460

8/22/2019

Uploaded through www.regulations.gov; **Docket ID No. EPA-HQ-OW-2018-0780.**
Comments Regarding National Primary Drinking Water Regulation for Perchlorate

The Massachusetts Department of Environmental Protection (MassDEP) appreciates the opportunity to comment on the United State Environmental Protection Agency's (USEPA) federal register notice entitled National Primary Drinking Water Regulations: Perchlorate: A Proposed Rule, Docket ID No. EPA-HQ-OW-2018-0780.

Perchlorate has been a priority drinking water contaminant issue for MassDEP for over a decade. In 2006 MassDEP adopted a drinking water standard or maximum contaminant level (MCL) of 2 micrograms per liter (ug/L) for perchlorate. This MCL was promulgated to address perchlorate toxicity to the developing fetal and infant brain. MassDEP has successfully implemented this standard since that time.

After nearly 21 years of assessment, USEPA is recommending a national MCL of 56 ug/L for perchlorate. This proposed limit is based on the output of a complex and uncertain computer model, and accepts an IQ loss of 2% among those exposed to perchlorate at this level. USEPA has requested comment on whether the target of acceptable IQ loss should instead be based on a 1% or 3% IQ loss, or whether the agency should conclude that no standard is warranted.

MassDEP disagrees with all of these options. Perchlorate has been shown to disrupt thyroid function through at least one mechanism of action involving inhibition of iodide uptake in the thyroid. Extensive human data demonstrates that chemical and physiological conditions that disrupt normal thyroid function can cause a range of adverse health effects. The developing neurological system in the fetus and infants is particularly sensitive to thyroid disruption. Considerable evidence from laboratory

experiments on animals and human epidemiological studies have reported perchlorate effects on the thyroid and on measures of neurological development.

MassDEP is alarmed that USEPA would consider a 2% or 3% IQ decrement, attributable to exposure of the fetus to a *single* contaminant in drinking water, as an acceptable health based target. Of the options presented, a 1% IQ decrement should be the maximum considered, which would be consistent with USEPA guidance, and which is also noted in the Federal Register Notice. The notice states that "(a) BMR [benchmark response] of 1% has typically been used for quantal human data from epidemiology studies". To our knowledge there is no regulatory precedent for determining that the IQ effect levels of 2-3% are acceptable. Indeed this policy decision is inconsistent with conclusions of the USEPA's Clean Air Scientific Advisory Committee (CASAC) in its consideration of the National Ambient Air Quality Standard (NAAQS) for lead, another neurotoxin, and with an assessment completed by the California Office of Environmental and Human Health Assessment (OEHHA) regarding lead in drinking water. Specifically, USEPA's CASAC concluded that a "population loss of 1-2 IQ points is highly significant from a public health perspective" (https://www.epa.gov/sites/production/files/2016-03/documents/finalrule_20081015presentation.pdf). Similarly, OEHHA chose a change of 1 IQ point as a benchmark target in a derivation of a health guidance value for lead in drinking water for use in health risk assessments at school sites.

MassDEP also wishes to emphasize a point appropriately noted in USEPA's documentation, that IQ is an incomplete measure of neurotoxicity and does not reflect other adverse outcomes, including various behavioral effects, associated with perchlorate exposure. These adverse outcomes can have highly significant impacts on individuals and society. This concern is reinforced in the USEPA Federal Register notice in Table III-2, which lists measures of neurological effects that are more sensitive to perchlorate than IQ. Some of the other effects associated with thyroid hormone deficits, as noted by USEPA in the Federal Register Notice, include ADHD, autism, and delayed cognitive development, among others. These end points represent significant potential for compromised health outcomes and negative public health measures that should be more robustly addressed.

USEPA has derived three alternative toxicity values (reference doses or RfDs) for perchlorate based on "acceptable" modeled IQ losses of 1, 2 or 3%. RfDs are an estimate of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

In its discussion of the proposed RfD options in the Federal Register, USEPA acknowledges numerous uncertainties inherent in its derivation of these values. These uncertainties are attributable to the many limitations of the complex biologically based dose response (BBDR) model used, and deficiencies in the data USEPA relied upon to predict perchlorate IQ loss. While MassDEP acknowledges that the BBDR model represents an advance that will help scientists better understand thyroid function and the potential effects of thyroid toxicants, it should be considered an experimental research tool with uncertain predictive utility. Some of the uncertainties in the model and the overall database are identified by USEPA in the Federal Register notice. The uncertainties USEPA identifies include:

1) **Relationship between exposure and outcome** ("uncertainty in the relationship between perchlorate exposure and subsequent neurodevelopmental outcomes");
2) **Limited toxicokinetic calibration data** ("very few toxicokinetic calibration data are available for the perchlorate to thyroid hormone relationship described in the BBDR model");
3) **Incomplete understanding of iodine depletion / intake levels and TSH compensation** ("aspects such as competitive inhibition at the sodium / iodide symporter (NIS), depletion of iodide stores under different iodine intake levels and physiological states, and the ability of the Thyroid Stimulating Hormone (TSH) feedback loop to compensate for perturbations in thyroid function each have their own uncertain features");
4) **Incomplete understanding of maternal** free Thyroxine **(fT4) level impacts on IQ and several factors impacting this relationship** ("uncertainties linking maternal fT4 levels to offspring IQ....(which) include the population for which dose-response information is available (i.e., no study is U.S. based), a lack of study information on the iodine intake status for the population for which the dose-response information is available, uncertainties around the methods used to assess maternal fT4 measurement during pregnancy, and uncertainties related to the true distribution of fT4 for a given iodine intake";
5) **Incomplete understanding of infant thyroid levels and outcomes** (".....some uncertainty due to the lack of information linking incremental changes in infant thyroid hormone levels to adverse neurodevelopmental outcomes");
6) **Incomplete understanding of fetal thyroid development after the first trimester** ("this analysis is assuming that protecting a first trimester fetus from alterations in maternal fT4 will protect the fetus throughout pregnancy" and "there is some uncertainty about the impact perchlorate may have on the fetal thyroid gland, and subsequent neurodevelopmental impacts, in later trimesters of pregnancy").

Although USEPA's materials present a daunting compilation of uncertainties, its list is not complete. USEPA's approach does not adequately account for data gaps relating to other potentially more sensitive effects. Neither does USEPA's approach address the fundamental uncertainty regarding perchlorate's mode of action, which may involve additional mechanisms such as effects on organification and thyroid hormone transport, in addition to competitive inhibition at the sodium iodide symporter (NIS).

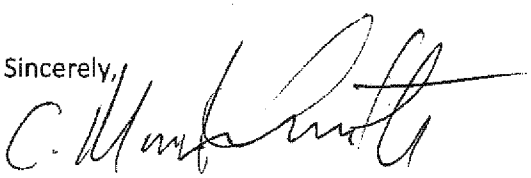
Toxicologists generally account for uncertainties such as these by applying uncertainty factors (UFs) in the derivation of RfDs. By convention and USEPA guidance, an UF of either 3 or 10 is applied to account for uncertainty in sensitivities and another factor of 3 or 10 to account for data gaps that might lead to an underestimate of effects. Despite the extensive list of highly significant uncertainties noted above, the USEPA applied a total UF of only 3 in its RfD derivations claiming this as sufficient to "account for the uncertainties in modeling the impacts of perchlorate ingestion on the thyroid hormone levels for pregnant mothers with low iodide intake, and the uncertainties in predicting the neurodevelopmental effects of these thyroid hormone changes on their children". MassDEP does not agree that this is sufficient. Given the range of USEPA's acknowledged uncertainties in multiple areas, as well as

additional uncertainties not addressed related to perchlorate's mode of action, an UF of 10 should be the minimum value applied and a factor of 30 could easily be justified.

If an UF of 10 is used with the USEPA proposed allowable IQ loss of 1%, a revised RfD of 0.31 ug/kg-day results. USEPA's perchlorate intake from food, derived as described in the Federal Register Notice, equals 0.45 ug/kg-day. This exceeds the more appropriate RfD alternative derived above (0.31 ug/kg-day). Using the more appropriate RfD of 0.31ug/kg-day and the USEPA default relative source contribution (RSC) factor (the fraction of the RfD allowed to come from drinking water) of 20% to derive an appropriate drinking water value, the result equals 1.9 ug/L. This value is much lower that the proposed MCL, and is close to the maximum contaminant level adopted by and implemented in Massachusetts.

In conclusion, MassDEP does not support USEPA's proposed options for addressing perchlorate in drinking water, which are likely to allow for significant adverse public health impacts. An MCL should be based on an assessment that fully addresses perchlorate's toxicity and uses appropriate, health protective uncertainty factors in its derivation. MassDEP urges the Agency to revise its proposal as suggested.

Sincerely,



C. Mark Smith Ph.D., M.S.

Director
Office of Research and Standards
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THE METROPOLITAN WATER DISTRICT
OF SOUTHERN CALIFORNIA

Office of the General Manager

August 23, 2019

Mr. Samuel Hernandez
Office of Ground Water and Drinking Water
Standards and Risk Management Division (Mail Code 4607M)
Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington, DC 20460

Dear Mr. Hernandez:

Comments on Docket ID No. EPA-HQ-OW-2018-0780, Proposed National Primary Drinking Water Regulation for Perchlorate

The Metropolitan Water District of Southern California (Metropolitan) appreciates this opportunity to comment on the U.S. Environmental Protection Agency's (EPA) proposed National Primary Drinking Water Regulation for perchlorate (84 Fed. Reg. 30524 (June 26, 2019), corrected 84 Fed. Reg. 33045 (July 11, 2019)). Metropolitan is a regional water wholesaler whose primary purpose is to provide its 26 member agencies with a safe and reliable water supply. Metropolitan imports water from the Colorado River, as well as from the State Water Project, and delivers it to its member agencies, which in turn directly or through their sub-agencies provide water to approximately 19 million people in Southern California. The lower Colorado River is a major drinking water source for not only Southern California, but also Arizona, Nevada, and northern Mexico.

Metropolitan disagrees with the fundamental assumptions that underlie EPA's proposed National Primary Drinking Water Regulation for perchlorate. Under the Safe Drinking Water Act, EPA should establish maximum contaminant levels (MCLs) for those contaminants that: 1) may have an adverse effect on public health, 2) are known to or likely to occur at levels of public health concern, and 3) in the sole judgment of EPA, regulation of the contaminant presents a meaningful opportunity for health risk reductions for persons served by public water systems. In this regard, Metropolitan offers the following comments:

1. Metropolitan recommends that, in setting an MCL for perchlorate, EPA consider the health effects data used for setting the MCLs and Advisory Levels for perchlorate by several states, as well as the rationale for setting those standards.
2. Metropolitan has concerns with EPA's underlying assumptions and analysis of national occurrence data for perchlorate. First, EPA does not have an up-to-date accounting of perchlorate contamination, either as a drinking water contaminant or from cleanup activities. Second, EPA excluded perchlorate data from California and Massachusetts which led to EPA's proposed 18 µg/L, 56 µg/L, or 90 µg/L MCL levels. Metropolitan recommends that EPA reanalyze national occurrence data for perchlorate, including data from California and Massachusetts.

Since the late 1990s, Metropolitan has been working to address perchlorate contamination of the Colorado River. In September 2009, Metropolitan submitted comments on the Perchlorate Supplemental Request for Comments (74 Fed. Reg. 41883 (Aug. 19, 2009)), emphasizing that a determination by EPA to regulate perchlorate in drinking water would help support cleanup efforts along the Colorado River and other contaminated sites. We continue to urge EPA to establish a drinking water regulation for perchlorate that is protective of human health and prevents any adverse impact to the Colorado River and the millions of users that rely upon it as a source of drinking water supply. As such, Metropolitan offers the following comments:

3. Metropolitan asks EPA to establish a drinking water standard for perchlorate that supports the ongoing remediation efforts and target cleanup goals at two chemical manufacturing facilities near Henderson, Nevada. Metropolitan, along with the Central Arizona Project (CAP), Southern Nevada Water Authority (SNWA), and the Nevada Division of Environmental Protection (NDEP), have been working cooperatively with EPA to address this long-standing issue, and the continuation of remediation at these sites is of paramount importance to the drinking water quality for the southwestern United States.
4. Metropolitan urges EPA not to withdraw its February 11, 2011, determination to regulate perchlorate in drinking water. If EPA withdraws its intent to regulate perchlorate, drinking water utilities in Nevada and Arizona which rely on Colorado River water could then have higher levels of perchlorate in their source water. The impact on California drinking water utilities would be even more significant because they may not be able to comply with California's existing maximum contaminant level (MCL) for perchlorate of 6 micrograms per liter (µg/L) and could be exposed to additional litigation and potential liability.

These four comments are described in further detail below.

1. **Metropolitan recommends that, in setting an MCL for perchlorate, EPA consider the health risk assessment process used by other states such as California in establishing MCLs and Advisory Levels for perchlorate. Metropolitan also recommends that EPA consider the monitoring and compliance guidance provided by California and Massachusetts in the development of their respective perchlorate drinking water regulations.**

California's MCL for perchlorate is 6 µg/L, effective October 2007. California's MCL for perchlorate is based on perchlorate's health risks, its detectability and treatability, and the cost of treatment. (Cal. Health & Safety Code § 116365(a), (b).) Thus, California considered many of the same factors that EPA is analyzing. Metropolitan encourages EPA to review the agency documents supporting California's MCL and Public Health Goal (PHG) for perchlorate, including the California Office of Environmental Health Hazard Assessment's (OEHHA) *Final Technical Support Document for Perchlorate in Drinking Water* (Feb. 2015) [1] and California Department of Public Health's (DPH) *Final Statement of Reasons, Perchlorate Primary Maximum Contaminant Level (MCL), Title 22, California Code of Regulations* (June 25, 2007)[2].

In setting the MCL for perchlorate, California found that the occurrence data indicated both a significant level of drinking water contamination and a potential for adverse health effects."[3] In February 2015, OEHHA lowered the PHG for perchlorate from 6 µg/L to 1 µg/L based on new research that focused on the effects of perchlorate on infants. The purpose of the reduced PHG of 1 µg/L is "to identify a level of perchlorate in drinking water that prevents perchlorate-related reductions in thyroidal iodide uptake and subsequent decreases in thyroid hormone production that may be associated with any of these adverse health effects." (OEHHA, *Final Technical Support Document for Perchlorate in Drinking Water* (Feb. 2015) at p. 158.) California Health and Safety Code Section 116365(a) requires the California State Water Resources Control Board (State Water Board) to set a primary drinking water standard for perchlorate that is as close to the PHG as is economically and technologically feasible.

As a result, on July 5, 2017, the Division of Drinking Water (DDW) recommended a two-step approach for possibly revising California's perchlorate MCL. First, DDW would lower the DLR from the current 4 µg/L concentration to a level closer to, equal to, or less than the PHG of 1 µg/L. With a revised DLR, new occurrence data can be collected to support the development of a revised MCL, if appropriate. Second, if supported by the new occurrence data, DDW would propose a new MCL as close to the 1 µg/L PHG as is technologically and economically feasible. The State Water Board approved DDW's proposal, and DDW is currently exploring the feasibility of establishing a lower DLR for perchlorate which might then result in a new, lower MCL for perchlorate of 1 µg/L or a level close to 1 µg/L.

Similarly, Massachusetts set an MCL for perchlorate of 2 µg/L in 2006. The chart below, which is adapted from OEHHA's *Final Technical Support Document for Perchlorate in Drinking Water*

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[1] Available at https://oehha.ca.gov/water/public-health-goal-fact-sheet/final-technical-support-document-public-health-goal-perchlorate.

[2] Available at https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/documents/perchloratemcl/R-16-04-FSOR.pdf.

[3] DPH, *Final Statement of Reasons, Perchlorate Primary Maximum Contaminant Level (MCL), Title 22, California Code of Regulations* (June 25, 2007) at p. 4.

(Feb. 2015) at page 156[4], shows the MCLs for California and Massachusetts and the Advisory Levels for other states with standards at the time of publication. (*Note: The standards for the states shaded in blue have changed since the publication date and have been updated herein)*:

State	Advisory Level	State	Advisory Level
Alabama	24.5	Missouri	10.9
Alaska	14	New Jersey	5
Arizona	11	New Mexico	13.8
California	1 (PHG) 6 (MCL)	New York	5
Florida	4	Nevada	18
Hawaii	15	North Carolina	2
Kansas	10.9	Texas	17
Maine	1	Vermont	1 (prevent) 2 (enforce)
Maryland	11	Virginia	15
Massachusetts	2 (MCL)	Wisconsin	0.1 (prevent) 1 (enforce)

In addition, EPA has a similar chart in its Technical Fact Sheet for Perchlorate which includes standards for the additional states of Colorado, Illinois, Indiana, Pennsylvania, Utah, and Wyoming. (EPA, *Technical Fact Sheet – Perchlorate* (Nov. 2017) at page 4.[5]) Notably, the standards for the states in these two charts range from 1 µg/L to 26 µg/L,[6] all of which are well below EPA's proposed MCL of 56 µg/L.

Metropolitan also recommends that EPA consider the monitoring and compliance guidance provided by California and Massachusetts in the development of their respective perchlorate drinking water regulations.[7] The guidance provides information on when water agencies need to monitor for perchlorate, what happens if perchlorate is detected, and when to monitor for

[4] Available at https://oehha.ca.gov/water/public-health-goal-fact-sheet/final-technical-support-document-public-health-goal-perchlorate.
[5] Available at https://www.epa.gov/sites/production/files/2017-10/documents/perchlorate_factsheet_9-15-17_508.pdf.
[6] EPA includes in its chart the non-residential standard of 71 µg/L for Kansas, but the residential standard is 11 µg/L.
[7] California's monitoring and compliance guidance for perchlorate is available at: https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/Perchlorate.html.

perchlorate again if no perchlorate is detected in the initial monitoring. (See Memorandum from California Department of Public Health to All Community and Nontransient-Noncommunity Water Systems (Oct. 12, 2007)[8].) California also provides information on minimum requirements for initial monitoring.[9]

2. **Metropolitan has concerns with EPA's underlying assumptions and analysis of national occurrence data for perchlorate: (1) EPA does not have an up-to-date accounting of perchlorate contamination, either as a drinking water contaminant or from cleanup activities; and (2) EPA excluded perchlorate data from California and Massachusetts which led to EPA's proposed 18 µg/L, 56 µg/L, or 90 µg/L MCL levels. Metropolitan recommends that EPA reanalyze national occurrence data for perchlorate while including data from California and Massachusetts.**

Metropolitan has two concerns with EPA's occurrence analysis: (1) EPA's reliance on older data from the first Unregulated Contaminant Monitoring Rule (UCMR 1) ignores other, more recent perchlorate occurrence data from around the country; and (2) much of EPA's analysis excludes data from California and Massachusetts.

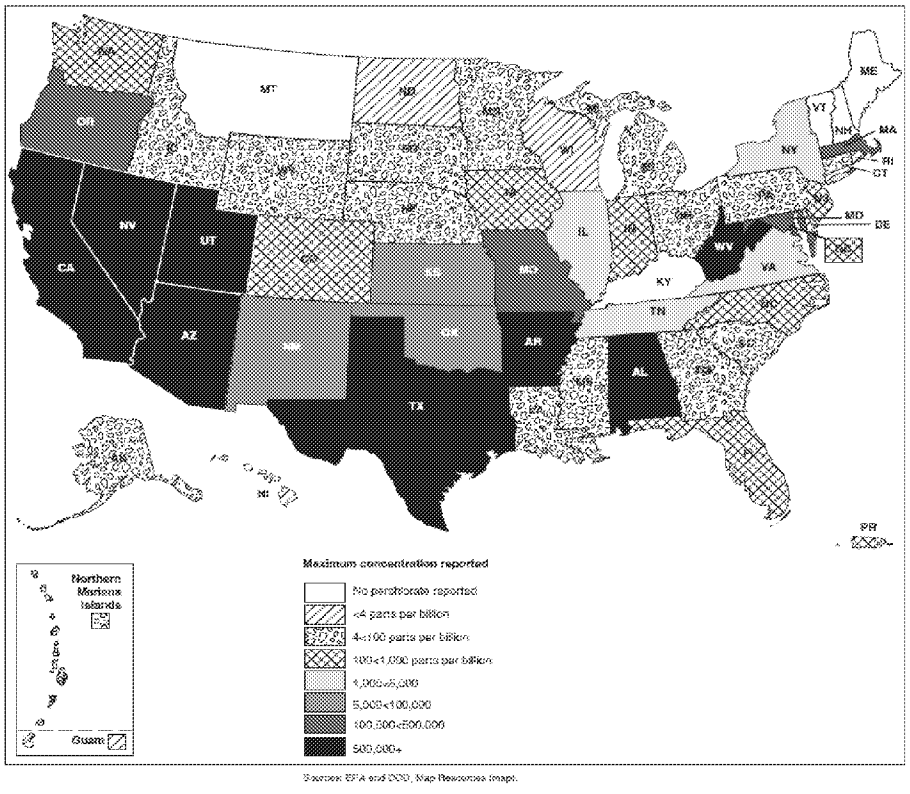
First, as EPA acknowledges, UCMR 1 data (which is based on monitoring conducted between 2001 and 2005) are "more than one decade old; actual occurrence could be lower (e.g., because of contaminant cleanup) or **higher** (e.g., because new systems use perchlorate-contaminated source water)." (84 Fed. Reg. at 30556 (emphasis added).) In fact, in 2005, the United States Government Accountability Office (GAO) recommended that EPA "establish a formal structure to centrally track and monitor perchlorate detections." (GAO, *Perchlorate: A System to Track Sampling and Cleanup Results Is Needed, GAO-05-462 (Washington, D.C.: May 20, 2005).*) EPA officials disagreed with that recommendation, saying that they "already had sufficient information on perchlorate concentrations in various environmental media that indicated the extent of contamination nationally and that if EPA were to implement a tracking system, the agency would require additional resources." (GAO, *Perchlorate: Occurrence is Widespread but at Varying Levels; Federal Agencies Have Taken Some Actions to Respond to and Lessen Releases, GAO-10-769 (Washington, D.C.: August 12, 2010)* ("GAO Report, '*Perchlorate Occurrence*'") at p. 9.) However, as GAO pointed out, "**[W]ithout a formal system to track and monitor perchlorate findings and cleanup activities, EPA and the states do not have the most current and complete accounting of perchlorate as an emerging contaminant of concern, including the extent of perchlorate found and the extent or effectiveness of cleanup projects**." (*Id.*, emphasis added) Yet the older UCMR 1 data is "the primary source of occurrence data the EPA relied on to estimate the number of water systems (and associated population) expected to be

[8] Available at https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/documents/perchlorate/AdoptionMemotoWaterSystems-10-2007.pdf.
[9] Available at https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/documents/perchlorate/Perchloratemonitoringchart-10-2007.pdf.

exposed at levels of perchlorate which could potentially exceed the proposed and alternative MCL levels." (84 Fed. Reg. at 30541.)

As an example of more recent occurrence data that EPA could have considered,[10] the Department of Defense (DOD) reported perchlorate detections at 284 of its installations, or almost 70 percent of the 407 installations sampled from fiscal years 1997 through 2009, with detections ranging from less than 1 µg/L up to 2.6 **million** µg/L. (*Id.* at p. 10.) In addition, as of June 2010, EPA reported perchlorate detections at 40 sites on the National Priorities List. (*Id.* at p. 12.) As EPA recognizes in its Technical Fact Sheet on Perchlorate, as of October 2009, perchlorate had been detected at varying levels in drinking water, groundwater, surface water, soil or sediment in 45 states, the District of Columbia, and three U.S. territories (see Figure 2 below).[11] (EPA, *Technical Fact Sheet – Perchlorate* (Nov. 2017) at p. 3.)

Figure 2: Maximum Perchlorate Concentrations Reported in Any Media as of October 2009



Second, Metropolitan does not concur with EPA excluding results from California and Massachusetts for perchlorate measurements that equal or exceed either 18 µg/L, 56 µg/L, or 90 µg/L simply "because water systems in these States must meet limits below 18 µg/L." (84 Fed.

[10] EPA cites this data in its Technical Fact Sheet on Perchlorate. (See EPA, *Technical Fact Sheet – Perchlorate* (Nov. 2017) at pp. 2-3.)

[11] Figure 2 is from GAO Report, *Perchlorate Occurrence*, page 13.

Reg. at 30542.) The fallacy of this assumption is shown by the fact that even though California has an MCL of 6 µg/L, 230 of 9,341 public water wells in California sampled between 2007 and 2017 had at least one detection of perchlorate above 6 µg/L. (State Water Board, *Groundwater Information Sheet: Perchlorate* (Nov. 2017).)[12] There were 173 groundwater sources in Los Angeles County (88), San Bernardino County (62), and Riverside County (23) alone that detected perchlorate above 6 µg/L. (*Id.*) In fact, California's OEHHA found that the results of a survey of "an essentially random sample of people from the U.S." suggested that "probably everyone in California, as well as everyone in the U.S., is exposed to perchlorate through some source." (OEHHA, *Final Technical Support Document for Perchlorate in Drinking Water* (Feb. 2015) at pp. 1, 152.)

Furthermore, perchlorate has been found in groundwater basins within Metropolitan's service area. The vast majority of locations where perchlorate has been detected in the groundwater are associated with the manufacturing or testing of solid rocket fuels for the DOD and the National Aeronautics and Space Administration (NASA), or with the manufacture, storage, handling, or disposal of perchlorate (such as at the Aerojet Rocketdyne site in Azusa, California and the Jet Propulsion Laboratory/NASA in Pasadena, California). Past agricultural practices using fertilizers containing naturally occurring perchlorate have also been implicated in some areas. According to the State Water Board's water quality database, monitoring results from 2011 to 2014 indicate that 17 of Metropolitan's 26 member agencies have detected perchlorate in their service areas at levels greater than 4 µg/L from groundwater sources. Thus, EPA's determination that there is an "infrequent occurrence of perchlorate at 18 µg/L, 56 µg/L, or 90 µg/L" (84 Fed. Reg. at 30541) is flawed because it is based on the exclusion of results from California and Massachusetts (84 Fed. Reg. at 30542). Metropolitan recommends that EPA reanalyze the occurrence data for perchlorate for the nation by including occurrence data from California and Massachusetts.

Also, the sources of perchlorate found in California and Massachusetts may be located outside of those states. As explained below, perchlorate in Orange County Water District's (OCWD) groundwater in California was traced to the Colorado River and found to originate from the two industrial sites near the Las Vegas Wash in Nevada. The Colorado River Basin includes the states of Nevada, Wyoming, Utah, Colorado, Arizona, and New Mexico. As shown above, none of these states have MCLs for perchlorate, and although some have Advisory Levels for perchlorate, most are higher than California's MCL of 6 µg/L. However, California's drinking water standard for perchlorate is not enforceable outside of the State. In addition, as shown on Figure 2 above, as of October 2009, several of the Colorado River Basin states had maximum perchlorate concentrations above 100 µg/L, some even higher than 500,000 µg/L. Protection of this source water is critical to the health and welfare of the residents in Southern California.

[12] Available at https://www.waterboards.ca.gov/gama/docs/coc_perchlorate.pdf.

Source water protection is critical to preventing perchlorate impacts not only to drinking water, but also to food. In 2004, the Food and Drug Administration (FDA) tested 500 samples of foods, including vegetables, milk, and bottled water for perchlorate. (Congressional Research Service, *Perchlorate Contamination of Drinking Water: Regulatory Issues and Legislative Actions* (Sept. 21, 2010) at pp. 1-2.) The FDA found perchlorate in approximately 90% of lettuce samples (average levels ranged from 11.9 µg/L to 7.7 µg/L), and in 101 of 104 bottled milk samples (with an average level of 5.7 µg/L). (*Id.* at p. 2.) The detection of perchlorate in food is relevant to EPA's rulemaking because EPA considers non-water exposures when determining whether to establish a standard for a contaminant and, if so, at what level. (*Id.*)

3. Metropolitan asks EPA to establish a drinking water standard for perchlorate that supports the ongoing remediation efforts and target cleanup goals at two chemical manufacturing facilities near Henderson, Nevada.

The Colorado River is a significant source of drinking water to approximately 19 million people in Southern California, as well as millions of people in Arizona, Nevada, and northern Mexico. Perchlorate was first detected in Colorado River water in 1997 and traced back to the Las Vegas Wash, which discharges into Lake Mead. The source of contamination was found to be emanating from two chemical manufacturing facilities near Henderson, Nevada: (1) a former Kerr-McGee facility which was owned by Tronox LLC and is now owned by the Nevada Environmental Response Trust (NERT); and (2) the former Pacific Engineering and Production Company of Nevada (PEPCON) site which was acquired by American Pacific Corporation (AMPAC) and is now operated by Endeavour, LLC. Under the oversight of the NDEP and EPA, there has been significant progress in reducing the loading of perchlorate into the Las Vegas Wash. At the time that perchlorate was first discovered, loading into the Wash was approximately 1,000 pounds per day, resulting in perchlorate levels exceeding 20 µg/L at times within Lake Mead. Interim remedial efforts have resulted in over a 90 percent reduction in perchlorate loading into the Las Vegas Wash, with levels decreasing from a high of 1,200 µg/L in 1998 to current levels between 50 and 70 µg/L on average. Further remediation is required to achieve greater reduction of perchlorate levels in the Wash. Due to ongoing cleanup activities, perchlorate levels in Lake Mead and the downstream Colorado River have typically remained below 2 µg/L over the past several years.

While the remedial efforts to date have been successful in reducing perchlorate loading into the Las Vegas Wash, a large perchlorate mass still remains at the Henderson sites. Groundwater at the NERT site contains high concentrations of perchlorate, up to 6,000 mg/L, and continues to migrate downstream towards the Wash and ultimately to the Colorado River. NERT is still conducting its remedial investigation of the site and downgradient areas and will then evaluate various long-term remedial alternatives. Currently, NERT is targeting groundwater cleanup to meet the interim federal drinking water health advisory level of 15 µg/L and Nevada's provisional action level of

18 µg/L (which is based on EPA's 1999 *Interim Assessment Guidance for Perchlorate*[13] (see NDEP's *Defining a Perchlorate Drinking Water Standard)*[14] within the Las Vegas Wash. EPA is working closely with NDEP to ensure that perchlorate releases to the Las Vegas Wash and Lake Mead are reduced effectively in a timely manner. Remedial construction of the long-term remedy for the NERT site is not expected to begin until late 2024/early 2025. Endeavour's long-term remedy, in operation since September 2012, has demonstrated a steady performance. Under the direction of NDEP, Endeavour has recently proposed modifications to their treatment system to remove perchlorate in surface drain waters not currently captured by their groundwater treatment system.

As an example of the Henderson sites' far-reaching impact, Metropolitan faces significant potential liability as a result of the perchlorate from the NERT site in Metropolitan's water supply. For example, in 2004, OCWD filed a lawsuit against several industrial defendants, alleging that they were responsible for contaminating OCWD's groundwater primarily with volatile organic compounds (VOCs). Subsequently, OCWD advised defendants that the remediation costs had increased considerably due to the presence of perchlorate in groundwater. In 2008, the defendants filed cross-claims against Metropolitan based on Metropolitan's sale of water containing perchlorate to OCWD for replenishment purposes. The source of the perchlorate in Metropolitan's Colorado River water was from the two chemical manufacturing sites near the Las Vegas Wash. Metropolitan incurred substantial costs defending itself in the case before trial. The trial was divided into phases, with the cross-claims against Metropolitan reserved for a later phase. At the end of the initial phase of the trial, the court ruled in favor of the industrial defendants. The appellate court subsequently reversed the judgment on two of OCWD's claims against one of the defendants, and affirmed the rest of the judgment. The case has been remanded to the trial court for further proceedings between OCWD and the remaining defendant. Thus, Metropolitan is still subject to potential cross-claims for the perchlorate cleanup costs.

In addition, because the target cleanup goal at the NERT site is based on EPA's 1999 *Interim Assessment Guidance for Perchlorate*, Metropolitan believes that EPA's proposed drinking water standard for perchlorate at 56 µg/L could adversely impact the ongoing cleanup efforts at the site. EPA's proposed MCL and MCLG of 56 µg/L are almost four times greater than the current target cleanup goal of 15 µg/L and could result in the cleanup goal being increased to a higher number. The alternative proposed MCL and MCLG of 90 µg/L are also much greater than the current target

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[13] In 2003, EPA re-affirmed its 1999 *Interim Assessment Guidance for Perchlorate* with an added suggestion "to carefully consider the low end of the provisional 4-18 ppb range." (Memorandum from EPA Assistant Administrator Marianne Lamont Horinko to Assistant Administrators and Regional Administrators, "Status of EPA's Interim Assessment Guidance for Perchlorate" (Jan. 22, 2003) (emphasis added).)

[14] Available at https://ndep.nv.gov/uploads/env-sitecleanup-active-bmi-perchlorate/perchlorate-drinking-water-standard.pdf.

cleanup goal. In fact, if the cleanup goal at the NERT site was revised to 90 µg/L, perchlorate levels may increase significantly in the Las Vegas Wash and in the downstream Colorado River.

EPA's alternative proposed MCL and MCLG of 18 µg/L are very close to the current cleanup goal at the NERT site of 15 µg/L and, thus, would likely not adversely impact site remediation efforts. Nevertheless, as explained in comment #1 above, it is possible that California's MCL for perchlorate could decrease to 1 µg/L or a level close to 1 µg/L in the near future. If so, it is even more important that EPA's MCL and the target cleanup goal at the NERT site be low enough so that appropriate remedial measures are in place to reduce perchlorate loading into the Las Vegas Wash. This will help enable water agencies in California to comply with any lower California MCL and possibly prevent their exposure to additional litigation and potential liability based on impacted Colorado River water quality.

Treating perchlorate contamination at the source in the Henderson, Nevada area is the most cost-effective way to protect public health rather than shifting that burden to millions of downstream Colorado River water users. Thus, given the negative impact that EPA's proposed MCLs of 56 µg/L and 90 µg/L could have on the remediation at the NERT site and the subsequent negative effect on downstream Colorado River water users, EPA's conclusion that "no alternative MCL, including the alternative MCL values of 18 µg/L and 90 µg/L . . ., would 'maximize health risk reduction benefits at a cost that is justified by the benefits'" (84 Fed. Reg. at 30557) is incorrect. For these reasons, EPA's proposed drinking water standard for perchlorate should take into consideration the long-term remediation of perchlorate contamination at the Henderson sites to a level that is protective of public health for downstream Colorado River water users and that helps achieve California's current and possible future MCL for perchlorate.

4. Metropolitan urges EPA not to withdraw its February 11, 2011, determination to regulate perchlorate in drinking water.

Metropolitan urges EPA not to withdraw its February 11, 2011, determination to regulate perchlorate in drinking water. If EPA withdraws its intent to regulate perchlorate, and subsequently, perchlorate treatment were to be discontinued at the Henderson sites, perchlorate levels in the Colorado River could revert to 9 µg/L in as little as 12 months. This level of perchlorate would impact drinking water utilities in Arizona and Nevada which rely on Colorado River water, and would result in California drinking water utilities that rely on Colorado River water not being able to comply with California's existing MCL for perchlorate of 6 µg/L, potentially exposing them to additional litigation and liability. The NERT site cleanup is funded solely from private funds obtained, in part, from the participation of Metropolitan, CAP, and SNWA in litigation in order to protect their source water and achieve compliance with the state regulations they are subject to. EPA, as the nation's environmental steward, should continue to support the efforts of NDEP to reduce the level of contaminants entering the Colorado River, a primary source of drinking water for over 25 million people.

Furthermore, federal regulation of perchlorate under the Safe Drinking Water Act (SDWA) is important to provide a source of funds to clean up perchlorate. For example, the purpose of the Drinking Water State Revolving Fund (DWSRF) program is to assist public water systems with financing the costs of infrastructure necessary to achieve or maintain compliance with SDWA requirements and to protect public health. Section 1452 of the SDWA authorizes EPA's Administrator to award capitalization grants to States, who in turn provide low interest loans and other types of assistance to eligible drinking water systems. If EPA decides not to regulate perchlorate in drinking water, this source of funds will not be available to water agencies that have to bear the financial burden of cleaning up perchlorate in their drinking water supplies. Metropolitan recommends that EPA regulate perchlorate in drinking water at a level that would support the current target cleanup goal of 15 µg/L for the NERT site.

As a regional water provider with source water originating in multiple jurisdictions, Metropolitan supports the federal regulation of perchlorate at a level that: (1) prevents drinking water contamination through source water protection; (2) is protective of public health for Colorado River water users; and (3) helps to achieve California's current and potential future MCL for perchlorate. EPA's role in establishing and enforcing a national drinking water standard for perchlorate will be critical in the long-term remediation of perchlorate contamination in the Colorado River Basin and hundreds of DOD sites around the country.

Metropolitan appreciates this opportunity to provide input to EPA on the various options for regulating perchlorate in public drinking water systems and requests that EPA carefully consider these comments. Please contact Dr. Mic Stewart, Metropolitan's Water Quality Section Manager, at (213) 217-5696 or mstewart@mwdh2o.com if you have any questions or need additional information.

Very truly yours,

Jeffrey Kightlinger
General Manager

cc: Mr. John J. Entsminger, General Manager
Southern Nevada Water Authority

Mr. Theodore C. Cooke, General Manager
Central Arizona Project

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT

Gavin Newsom, Governor
Jared Blumenfeld, Secretary for Environmental Protection
Lauren Zeise, Ph.D., Director

August 23, 2019

Samuel Hernandez
Office of Ground Water and Drinking Water, Standards and Risk Management Division
Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington, DC 20460

Re: comments on proposed perchlorate Maximum Contaminant Level, Docket No. EPA-HQ-OW-2018-0780

Dear Dr. Hernandez:

The Office of Environmental Health Hazard Assessment in the California Environmental Protection Agency is pleased to provide comments on the U.S. Environmental Protection Agency's proposed Maximum Contaminant Level (MCL) for perchlorate in drinking water (Federal Register of Wednesday, June 26, 2019 (84 FR 30524) (FRL-9994-68-OW).

The California Office of Environmental Health Hazard Assessment (OEHHA) believes that the Maximum Contaminant Level Goals (MCLGs) and Maximum Contaminant Levels (MCLs) recently proposed by the US Environmental Protection Agency (US EPA) for perchlorate (US EPA, 2019) are not adequately health-protective. In developing these levels, US EPA has taken approaches in a number of important areas that are not fully justified, not appropriate, and that need to be reconsidered. We have a large number of concerns with the proposed MCLGs and MCLs and the methods used to develop them. Our key areas of concern are described below.

Comments on the US EPA Proposed MCL/MCLG for Perchlorate

I. PBPK/PD MODEL: ASSUMPTIONS AND VALIDATION

A. The model is complex, includes a number of assumptions and is not reviewable without additional information

The US EPA proposal is based on a physiologically based pharmacokinetic/pharmacodynamic (PBPK/PD) model (coupled with a dose-response model) that is extremely complex (US EPA, 2017a). While we understand the reasons for attempting to link perchlorate exposure with hypothyroxinemia and neurodevelopmental outcomes, and appreciate the effort that has gone into developing the biologically-based dose-response (BBDR) model, the complexity of these models and the lack of documentation to support them result in a significant lack of transparency. More specifically, the US EPA proposal itself does not provide adequate justification or documentation for many of the assumptions used in the models or the approaches US EPA has used to attempt to validate these models. Because of this lack of information, it is extremely difficult to interpret the validity of the models, and it is not possible to fully evaluate them or to provide very specific comments on the modeling process in the timeframe US EPA has provided for public comment. Overall, based on this lack of transparency, we do not feel it is appropriate for US EPA to use these models as the primary basis of their proposed standards at this time.

B. Model validation

Importantly, the PBPK/PD model US EPA is proposing to use has not been validated for the most sensitive subpopulations: pregnant women, their fetuses, and infants. Calibration or validation with healthy non-pregnant adults is not appropriate since, as noted by US EPA, healthy non-pregnant adults are not one of the more susceptible groups. Comparisons to short-term dosing studies (e.g., Greer et al., 2002) are also problematic since adults have several months of stores of thyroid hormone, and these stores can temporarily mask any deficiency in thyroid hormone production that may be caused by perchlorate. Calibration or validation using animal data is not especially suitable since key aspects of the hypothalamic-pituitary-thyroid axis and key aspects of neurodevelopment differ markedly between species.

Although US EPA appears to have compared some aspects of the model to data from some human studies, the major outcomes of the model (e.g., the impacts of perchlorate on free thyroxine (fT4) levels) or critical precursor events (e.g., thyroidal iodide uptake) have not been shown to match the results of research studies in the most sensitive

groups. For example, in an independent analysis by Clewell et al. (2019), predictions from the US EPA PBPK/PD model were compared to the results of four studies in humans; only two of these studies involved pregnant women and none involved young infants. One of the studies in pregnant women (Téllez Téllez et al., 2005) used by Clewell et al. to compare to US EPA's modeling results was essentially an ecologic design, involving pregnant women with iodine levels that were much higher than commonly seen in the US, and took place in parts of Chile that had well- documented high exposures to other toxic agents (Cortés et al., 2016; Hopenhayn et al., 2003). Thus, this comparison is not particularly informative. In the other comparison, using by far the largest study in pregnant women (Steinmaus et al., 2016), the risks of declining thyroid hormone levels associated with perchlorate were under-predicted by the US EPA model by up to 100-fold. The key advantages of this particular study were: its large size; statistically significant results; consistency of effects for fT4, total thyroxine (T4), and thyroid stimulating hormone (TSH); inclusion of pregnant women from the US; and availability of information on a wide range of potential confounding variables such as iodine status, anti-thyroid antibodies, and socioeconomic indicators (Steinmaus et al., 2016). US EPA provides no explanation why its model so severely under-predicts this human research study. Overall, we feel it is inappropriate for US EPA to rely on a model that has not been adequately validated and that produces risk estimates that are far below those of the largest study to date on perchlorate and thyroid hormones in pregnant women.

II. INADEQUATE INCORPORATION OF UNCERTAINTY

One of the key areas of uncertainty noted by US EPA is the variation and uncertainty in the relationship between exposure and response among the members of the human population, that is, intraspecies variability. In developing its proposed MCLGs/MCLs, US EPA applied an intraspecies uncertainty factor of 3 to the point of departure (representing a 2% drop in IQ) to arrive at a reference dose. Typically, US EPA uses a default intraspecies uncertainty factor of 10. While regulatory agencies often decrease the toxicokinetic component of the intraspecies uncertainty factor when PBPK/PD modeling is used, the use of complex PBPK/PD models with a large number of assumptions does not necessarily reduce uncertainty.

In its 2005 review, an expert committee of the National Research Council recommended that US EPA use a factor of 10 to account for uncertainty in developing its perchlorate reference dose (NRC, 2005). This was consistent with US EPA guidelines that also call for a default uncertainty factor of 10 for intraspecies uncertainty (US EPA, 2002). In addition, US EPA's previous reference doses and its previous health advisories for perchlorate have used this same uncertainty factor (US EPA 2008a and 2008b).

Importantly, each of these previous documents and recommendations involved a reference dose that was based on human data (albeit in nonpregnant adults and using short-term exposure), not estimates from complex and uncertain models. A number of other experienced regulatory bodies have also used or recommended an uncertainty factor of 10 or higher in their perchlorate risk assessments (MassDep, 2006; OEHHA, 2015; New Jersey DEP, 2006).

In spite of these guidelines and recommendations, and without, in our view, adequate justification or supporting information, US EPA has decided to lower its intraspecies uncertainty factor from 10 to 3. For the reasons described below, we believe this decision is unjustified and not health-protective.

First, in its 2002 guidance document, "A Review of the Reference Dose and Reference Concentration Process," US EPA recommends reducing the intraspecies uncertainty factor from a default of 10 "only if data are sufficiently representative of the exposure/dose-response data for the most susceptible subpopulation(s)" (US EPA, 2002). Importantly, the information US EPA is using to develop its proposed MCLGs/MCLs is not from actual susceptible human populations. Rather, the information forming the basis of their assessment comes from estimates developed from models that have a large number of parameters, lack transparency, have considerable complexity, have not been adequately validated, and which therefore are associated with considerable uncertainty. Further, as mentioned above, the model severely underpredicts the effects seen in Steinmaus et al. (2016), the largest study of perchlorate in pregnant women to date. Based on all of these issues, there is no reason to believe that US EPA's model predictions are "sufficiently representative of the exposure/dose-response data for the most susceptible subpopulation(s)", and thus provide no valid justification for reducing the intraspecies uncertainty factor from the default level of 10.

Second, US EPA chose a point of departure "designed to provide an adequate margin of safety for the fetuses of mothers with an fT4 at the 10^{th} percentile of a population, an iodine intake of 75 µg/day, and a TSH feedback loop that is less than 60% as effective as individuals with a median TSH feedback loop efficacy." In deciding to model populations with an iodine intake of 75 µg/day, US EPA rationalizes that: "This value represents an intake between the 15th and 20th percentile of the women of child bearing age population distribution of estimated iodine intake from the National Health and Nutrition Examination Survey (NHANES). The EPA considered using a lower iodine intake level of 50 µg/day, which represents approximately the 5th percentile of the NHANES distribution. At 50 µg/day of iodine intake, however, the BBDR model predicts TSH levels that would be elevated to within the clinically hypothyroid range before

exposure to any perchlorate. In contrast, at 75 µg/day iodine, the BBDR modeled concentrations of serum fT4 and TSH are significantly reduced from the population median but are still within the euthyroid range." We see a major problem with this approach. That is, by choosing not to model women who are hypothyroid or women with low iodine intakes (i.e. below 75 µg/day), US EPA is essentially excluding two groups of women that are likely to be at very high risk from exposure to perchlorate. As such, US EPA's statement that an uncertainty factor of 3 is appropriate because the point of departure is based on the most sensitive members of the population of pregnant women is not justified.

Third, by attempting to include factors such as iodine intake, low baseline fT4 levels, or inter-individual differences in the sensitivity of the thyroid hormone feedback loops into their PBPK/PD model, US EPA has tried to incorporate some aspects of inter-human variability into their proposed MCLGs/MCLs. However, since the model has not been fully validated and since it is based on several questionable parameters, it is unknown whether any of these particular factors have truly been accounted for. As such, considerable uncertainty related to each of these remains.

Fourth, there are a number of other areas of uncertainty and potential areas of increased susceptibility that are not incorporated into US EPA's proposed MCLGs/MCLs. Some of these are specifically acknowledged by US EPA (pages 52-53), including uncertainty related to:

- Inter-individual differences in the competitive inhibition at the sodium iodide symporter (NIS)
- The depletion of iodide stores under different iodine intake levels and physiological states
- The lack of dose-response information linking fT4 to IQ from the US
- A lack of full information on the iodine intake status of the population used to estimate the dose-response relationship between maternal fT4 and childhood IQ
- The methods used to assess maternal fT4 measurement during pregnancy
- The true distribution of fT4 for a given iodine intake
- The possibility of sensitive life stages other than the first trimester fetus
- The lack of information linking incremental changes in infant thyroid hormone levels to adverse neurodevelopmental outcomes
- The potential role of the low levels of iodine storage in the fetus and infant
- The potential role of iron deficiency and its relationship to hypothyroxinemia in pregnant women
- The role of exposure to other chemicals that, like perchlorate, can also inhibit iodide uptake into the thyroid gland including nitrate (from drinking water and food) and thiocyanate (from food and tobacco smoke). These very common chemicals may have additive or synergistic effects with perchlorate in women or neonates who are co-exposed

- Uncertainty as to whether US EPA's incorporation of the variability in fT4 responses to TSH adequately reflect the true variability in the population.

Several other areas of uncertainty exist, and these are also not incorporated into US EPA's proposed MCLGs/MCLs. These include:

- Co-exposure to chemicals, including a number of pesticides or common industrial contaminants such as polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs), bisphenol A, and per-/polyfluoroalkyl substances (PFAS), that may alter thyroid hormone levels or thyroid function by mechanisms other than thyroidal iodide uptake inhibition.
- Susceptibility due to other pre-existing thyroid diseases or the presence of anti-thyroid antibodies (thyroglobulin antibody and thyroid peroxidase antibody). US EPA has attempted to incorporate susceptibility related to low baseline values of fT4, but as mentioned above the models are still based only on euthyroid women. Importantly, not all pregnant women are euthyroid. (As noted above, US EPA did not model women who were hypothyroid, only those with hypothyroxinemia in the first trimester). Overall, there are many thyroid conditions that could affect an individual's susceptibility to perchlorate, and it is unlikely that US EPA has accounted for a number of them.
- Misclassification of fT4 levels in the Korevaar et al. (2016) study linking maternal fT4 to offspring IQ. Free thyroxine levels were only measured at a single point in time in this study. However, thyroid hormone levels can fluctuate over time, and pregnancy is a period of major changes in thyroid hormone levels (Lambert-Messerlian et al., 2008). As such, a single measurement of fT4 may not accurately reflect true long-term thyroid hormone status. Additional misclassification can occur due to the changes in binding protein levels that take place during pregnancy. These changes are known to adversely affect the test used to measure fT4 (Sapin and d' Herbomez, 2003). Because misclassification due to these factors is unlikely to be related to neurodevelopment, the resulting bias is most likely towards the null, that is, towards finding a weaker relationship between maternal fT4 and childhood IQ than what actually exists. Correcting for this bias would most likely increase the fT4-IQ association reported by Korevaar et al. and thus most likely decrease the reference dose and MCLGs/MCLs proposed by US EPA.

In conclusion, considerable uncertainty is present in the proposed MCLGs/MCLs but US EPA presents little justification for lowering its intraspecies uncertainty factor by >300%. Its decision to use such a low uncertainty factor is inconsistent with its own recommendations and past practices as well as the recommendations and past practices of other experienced agencies and experts. As we have described above, a large number of uncertainties exist in US EPA's proposed approach, and we do not agree that all, or even most, of them have been accounted for. Thus, we do not agree with applying an uncertainty factor of 3. Rather, at a minimum, the uncertainty factor should be 10.

III. THE USE OF A SINGLE STUDY ON NEURODEVELOPMENT

A. Other endpoints are not considered

In its most recent review, an expert committee of the National Research Council identified inhibition of iodide uptake by the thyroid and subsequent thyroid deficiency as the primary mode of action of perchlorate, and stated that, "...if it does not occur, there is no progression to adverse health effects" (NRC, 2005). By choosing a critical early effect like this as the basis for risk assessment and standard setting, all of the potential adverse effects that result from it, both known and unknown, should be prevented. Based on this principle, the NRC committee concluded that the "use of inhibition of iodide uptake by the thyroid as the basis of the perchlorate risk assessment to be the most health-protective and scientifically valid approach." The fact that there may be currently unknown or poorly described consequences of NIS inhibition and thyroid deficiency does not seem to have been considered by US EPA. The functions of thyroid hormone are complex and multi-faceted, and it is likely that there are a number of unknown or not yet well-described adverse effects of thyroid deficiency and perchlorate exposure.

In its draft proposal however, rather than using iodide uptake inhibition, US EPA now bases its MCLG/MCLs on a single downstream event, IQ loss. While we acknowledge that IQ loss is an important endpoint, it is unknown whether this is the most sensitive endpoint. In other words, it is unknown whether protecting against this particular outcome will help protect against all or even most of the other potential adverse outcomes that could be caused by perchlorate. Thyroid hormone is involved in many important physiological processes and plays a role in a number of important adverse events ranging from cardiovascular disease to alterations of digestive and muscle function to deficiencies in neuro- and physical development. Neurodevelopment is also complex and multifaceted, and we are not aware of any evidence suggesting that a single metric like IQ accounts for all aspects of this highly complicated process. By basing its MCLG/MCLs on a single highly specific downstream event like IQ, rather than on a very well-documented and relatively easily measured critical precursor event like iodine uptake inhibition, it seems likely that US EPA's current approach could have missed some of the more sensitive effects of thyroid deficiency and perchlorate.

B. The most sensitive neurodevelopment endpoint may not have been selected

With regards to neurodevelopment, US EPA identified five papers and seven analyses that they found useful for estimating the dose-response relationship between maternal fT4 and neurodevelopment. The outcomes assessed varied from study to study and included IQ, Mental Development Index (MDI), and Psychomotor Development Index (PDI), anxiety/depression scores, and reaction time. Of the five studies and seven analyses, US EPA selected its own re-analysis of a single study, the investigation of childhood IQ by Korevaar et al. (2016). For several reasons, we believe the use of this study by US EPA as its sole source of information on the fT4-neurodevelopment relationship is inappropriate and not adequately justified.

First, except for the Finken et al. (2013) study involving reaction time, the Korevaar et al. study had the least conservative dose-response slope of any of the seven analyses considered by US EPA. For example, the slope US EPA derived using the Korevaar et al. data was 3.5 times lower than that reported in the study of maternal fT4 and offspring PDI of Pop et al. (1999). If the goal is to develop an MCLG or MCL that is appropriately health protective, selection of a study with one of the least sensitive endpoints will not achieve this goal. It should also be noted that the urinary iodine levels in the women in the Korevaar et al. study appeared to be much higher (227 µg/g creatinine) than levels typically seen in US pregnant women. As such, the findings of this study may not be representative of much of the US.

Second, several of the studies of fT4 and a neurodevelopmental outcome were excluded for reasons that were difficult to follow. For example, US EPA decided not to use one study because the measured endpoint of "anxiety/depression is not an intuitively interpretable endpoint," without explanation of what is meant by "intuitively interpretable." In addition, a study of maternal hypothyroxinemia and cognitive and behavioral deficits in children by Vermiglio et al. (2004) was discussed extensively in a previous US EPA document on perchlorate (US EPA, 2017b) but is not even cited in the draft proposal. This omission is important because the magnitude of the association between fT4 and IQ reported by Vermiglio et al. was almost four times greater than that reported by Korevaar et al. (US EPA, 2017b).

US EPA appears not to have used the Pop et al. (1999) and Pop et al. (2003) studies because of their small sample sizes and because neither was adjusted for confounders. However, sample size was not a major problem with either study since both were large enough to identify findings that were statistically significant. As noted previously by US EPA, "a small study that does detect an association is notable given the lack of power that is associated with a small sample size" (US EPA, 2017b). Further, it is not appropriate to exclude a study based on confounding without doing an adequate evaluation of this bias. While there are a number of methods to do this (see Axelson,

1978 as an example), none of these are presented in the draft proposal. For example, we note that while the results of Pop et al. (1999) using fT4 and PDI as continuous variables were not adjusted, categorical analyses presented in this study showed that a strong association between fT4 and PDI remained after adjustment for education, smoking, anti-thyroid antibodies, maternal depression, and other factors. In Pop et al. (2003), women with depression, obstetrical complications, or clinical or subclinical thyroid conditions, and children with low birth weight or hospitalizations were excluded. These exclusions should have removed any important confounding caused by each of these factors. For other variables, such as maternal and paternal education levels, smoking, alcohol intake, income, breastfeeding, birth weight, and gestational age, major differences were not seen between women with low and high fT4 levels in this study, suggesting that confounding by these variables is unlikely. These are a few examples of the types of analyses that can be done to evaluate confounding but they do not appear to be a part of the development of the proposed MCLGs/MCLs.

The two Pop et al. papers discussed above assessed the impacts of maternal fT4 and neurodevelopment using the Bayley Scales of Infant Development. US EPA has previously described these scales as, "the gold standard for neurodevelopmental assessment of children" and "a reliable indicator of the current development and cognitive functioning of the infant" (US EPA, 2017c). The MDI scale of the Bayley test evaluates aspects of functioning such as eye hand coordination, manipulation, understanding of object relations, imitation, and early language development. The PDI scale of the Bayley test assesses gross motor development. While the ability of the Bayley scales in young children to predict future outcomes may not be as strong as IQ in later life, this does not mean that the Bayley scales are not important. Rather, they are a commonly used metric for assessing early life development and several studies have shown that they have at least some predictive value for future outcomes (Siegel, 1982; Van Baar and de Graaff, 1994; Van Wassenaer et al. 1997; Luttikhuizen dos Santos, 2013). By excluding the two Pop et al. studies for reasons that are not clear, US EPA may have unjustifiably excluded two valid sources of information on outcomes that could be more sensitive than IQ.

Categorical data can also be used for risk assessment, and US EPA identified a number of studies using categorical data that reported fairly clear associations between thyroid deficiency and neurodevelopment (US EPA, 2017b). In fact, in an earlier document, US EPA noted that out of the 13 studies (and two meta-analyses) it identified that used categorical data, 11 found evidence for an association (US EPA, 2017b). However, none of these studies were used to develop the proposed MCLG/MCLs. Studies or analyses involving thyroid hormones other than fT4, specifically thyroid stimulating hormone (TSH), studies of other thyroid disorders (e.g. hypothyroidism), and studies not

involving the first trimester of pregnancy were also not used. These exclusions may have also led to some sensitive outcomes being missed. For example, based on its earlier PBPK/PD modeling, US EPA estimated that the drinking water level of perchlorate estimated to cause a 10% increase in TSH was 3 µg/L. This is 19 times lower than the currently proposed MCLG/MCL of 56 µg/L (US EPA, 2017b) which is based solely on fT4. And, in its 2017 methodology paper on perchlorate, US EPA calculated a point of departure (POD) of 0.4 µg/kg-day for a one percent increase in the number of women with hypothyroxinemia. This is 17 times lower than the POD of 6.7 µg/kg-day US EPA used to calculate the proposed MCLG/MCL of 56 µg/L (US EPA, 2017b). Overall, by essentially ignoring all of these other studies and other outcomes, it is very likely that US EPA's proposed MCLGs/MCLs are not based on the most sensitive adverse effect.

In summary, while US EPA identified several different studies of fT4 and neurodevelopment, it has selected an endpoint that gives one of the least sensitive dose-response relationships and therefore inappropriately high MCLGs/MCLs. The main reasons why US EPA appears to have made this selection is that IQ is "intuitively interpretable," and that the Korevaar et al. study had a large sample size. However, neither of these factors means that the outcomes assessed in the other studies are not relevant, valid, or important. In order to help assure that the most sensitive known outcome is considered, we believe that US EPA should reconsider the information on the other studies of thyroid hormone and neurodevelopment it has identified. As shown in Table III-2 of the draft document (US EPA, 2019), use of the data by Pop et al. (1999 and 2003) would result in a reference dose that is approximately 3-times lower than that currently proposed by US EPA. This type of major difference in sensitivity should not be ignored if the goal is to develop an MCLG/MCL that is truly health-protective.

C. Re-analysis of original study findings by Korevaar et al. is not justified

Despite describing the original Korevaar et al. (2016) study as "the most rigorous analysis available in the literature to date," US EPA reanalyzed the Korevaar et al. data and used the results of this re-analysis in their models. This re-analysis was done in response to a peer review comment questioning the fit of the log-linear model originally used by Korevaar et al. and questioning whether the addition of certain variables in the model "may have driven [biased] measures of association towards the null." We agree with this reviewer's concerns in principle. However, the re-analysis done by US EPA did not result in an association that was further away from the null as the reviewer (and we) expected. Rather, the opposite occurred: the change in fT4 needed to cause a 1% decrease in IQ was 62% **higher** in US EPA's re-analysis than that originally reported by Korevaar et al. Overall, while we agree that model overfitting can sometimes be a

problem, in order to be fully transparent US EPA needs to show that the variables they removed from the original Korevaar et al. model really did cause overfitting and were not actual confounders. US EPA should also provide more information on whether or not their new model provides a better fit than the original model, and provide a rational explanation of why their re-analysis produced results that were in an unusual and unexpected direction. We do not feel it is appropriate for US EPA to use the results of their re-analysis of the Korevaar et al. data until these issues are adequately addressed.

IV. OTHER SUSCEPTIBLE GROUPS: INFANTS

Based on the recommendation of its Scientific Advisory Board, US EPA decided to focus on fetuses of hypothryoxinemic first-trimester pregnant women as the most sensitive subgroup. Importantly though, there are other sensitive subgroups and none of these have been included in US EPA's MCLG/MCL development.

The decision to focus solely on this group appears to be based on the assumption that the relationship between thyroid deficiency and adverse neurodevelopment is greatest during the first trimester fetal period. While we acknowledge that there is some evidence to suggest this may be the case, this evidence is far from conclusive, and a variety of other research suggests that thyroid function is critically important during other life stages. For example, in Pop et al. (2003), while maternal fT4 levels in the first trimester were strongly linked to neurodevelopmental outcomes in the offspring, this effect only occurred when maternal fT4 levels continued to remain low into the 2nd or 3rd trimesters. This highlights the importance of thyroid hormone throughout the entire pregnancy, not just during the first trimester.

A wealth of research also shows that adequate thyroid function in the neonatal and later infancy periods is important for neurodevelopment (Zoeller and Rovet, 2004). And, as reviewed by OEHHA (2015), several research studies have linked perchlorate to changes in thyroid hormone levels in young children (Steinmaus et al., 2010; Brechner et al., 2000; Kelsh et al.,2003; Buffler et al., 2006; Li et al., 2000; Crump et al., 2000). Even US EPA's own models have identified young infants as a major susceptible subpopulation. For example, in US EPA's 2009 PBPK/PD model, inhibition of iodide uptake into the thyroid gland at a given drinking water level of perchlorate was predicted to be about four times higher in bottle fed infants than in first trimester pregnant women (US EPA, 2009). Overall, based on all of this evidence, it seems highly unlikely that the impacts of thyroid deficiency on neurodevelopment completely disappear after the first trimester of pregnancy, and therefore it is unreasonable not to consider neonates or young infants as an important susceptible subpopulation.

Consideration of neonates or young infants is especially important because perchlorate intake on a per body weight basis at a given concentration of perchlorate in drinking water is markedly higher (almost six times higher) in bottle-fed infants than in first-trimester pregnant women (OEHHA, 2015). This fact does not seem to have been considered in US EPA's most recent proposal. Young infants may also be particularly susceptible to perchlorate because they have much lower levels of stored thyroid hormone than adults. These low reserves likely make infants much more susceptible than adults to any short-term reductions in thyroid hormone production that could be caused by perchlorate.

It appears that US EPA decided to exclude infants based on an earlier BBDR model and the assumption that iodine in infant formula would offset the effects of perchlorate. However, to our knowledge neither the results of this earlier model nor the assumption regarding iodine in formula have not been validated or confirmed. OEHHA's latest perchlorate Public Health Goal (OEHHA, 2015) used bottle-fed infants as the most susceptible subpopulation, and included a specific drinking water intake rate for bottle-fed infants. By not considering the much higher drinking water intakes rates in neonates and infants, and by not fully considering the risks in these young children, it is highly likely that US EPA's proposed MCLG/MCLs are not adequately protective for these important susceptible subpopulations.

V. A BENCHMARK RESPONSE OF 2% IS NOT HEALTH PROTECTIVE

The primary MCLG and MCL of 56 µg/L proposed by US EPA are based on a two-point (or 2%) loss in IQ, that is, a benchmark response (BMR) of 2%. An approach using a BMR of 1% is provided as an alternative, and this results in an MCL that is three times lower (the MCL is not directly proportional to the BMR because the relative source contribution of perchlorate from food is increased when lower BMRs are used). Importantly, US EPA provides no justification for why it selected a BMR of 2%. The US EPA's benchmark guidance notes that when assessing animal toxicological data, as a starting point the analyst might consider a benchmark response rate for continuous data as one standard deviation. In the case of IQ, that would be 15 IQ points, obviously not a good benchmark response rate for such an important outcome. In the draft proposal, US EPA states that it looked to its 2012 Benchmark Dose Guidance document for insight and specifically noted that, "[a] BMR of 1% has typically been used for quantal human data from epidemiology studies." (US EPA, 2012). While the guidance document does not recommend a specific BMR for continuous data, we see no reason why this recommendation should differ between quantal and continuous human data, particularly for an endpoint such as IQ.

The guidance document goes on to state that, "The ideal is to have a biological basis for the BMR for continuous data, e.g., a consensus scientific definition of what minimal level of change in a continuous endpoint is **biologically significant."** While a 1% decrease in IQ in an individual may or may not be noticeable, a 1% decrease in the average IQ in a large population certainly is *biologically significant*. For example, Bellinger (2004) has shown that while relatively small changes in IQ associated with lead exposure may have limited impacts at the individual level, they can cause major increases in the numbers of people at the low end of the IQ spectrum and major decreases in the numbers of people at the higher end of the IQ spectrum. Weiss has shown that this effect is even greater in disadvantaged populations (Weiss, 2000). Like lead, perchlorate exposure is widespread. That is, essentially everyone in the US is exposed (Blount et al., 2007), and in its draft document US EPA estimates that 4-16 million people may have perchlorate concentrations ≥4 µg/L in their drinking water. Given this widespread exposure, small changes in IQ due to perchlorate, including a 1% change, can have major population impacts and therefore should be considered biologically significant. As such, if IQ or any other major neurologic outcome is used as the basis of the MCLG/MCL, at a minimum, a 1% change should be selected as the BMR.

VI. SUMMARY

US EPA has made a number of key decisions that are not well supported and which have resulted in proposed reference levels and MCLGs/MCLs that are higher than the health- protective levels it has previously proposed and higher than those proposed by other agencies and experts. This includes its decision to use a model that is exceedingly complex and opaque, has not been appropriately validated, and which is associated with considerable uncertainty. It also includes its decisions to lower its uncertainty factor to a level markedly below its well-established default value, its decision to use a benchmark response that is higher than what most would consider biologically significant, and its decisions to not use the most sensitive endpoints or populations. Given these concerns, we would like to make the following recommendations:

1. US EPA should not use its current PBPK/PD model unless and until all parameters are well justified, it can be made more transparent (see Clewell et al., 2019), and it is appropriately calibrated and validated.
2. These parameters and this validation should be based on data from the most susceptible groups including pregnant women, fetuses, and young infants. We acknowledge that the appropriate data from fetuses for validation and calibration may never be available. This is a major underlying flaw in the PBPK/PD model that might never be overcome.

3. US EPA should use an intraspecies uncertainty factor of at least 10 in order to more appropriately account for sensitive populations besides the fetuses of pregnant women in the first trimester. These include bottle-fed infants, fetuses of pregnant women who are not euthyroid, women with very low iodine intakes, and other individuals with thyroid disease.
4. US EPA's benchmark response should be based on the most sensitive outcome or on a sensitive critical precursor event such as inhibition of uptake of iodide by the thyroid. The latter is the best way to help assure that all important adverse effects, both known and unknown, can be prevented.
5. If IQ or a similarly important outcome is selected as the critical event, a 1% decrease is likely to be biologically significant and should therefore be used as the benchmark response, rather than 2% IQ loss as in the current US EPA proposal.
6. US EPA should not use re-analyzed data (e.g., the Korevaar et al. analysis) unless the re-analysis is fully justified, the methods and results are transparent, and any discrepancies or unusual results are explained.
7. Neonates and infants should be considered a susceptible group and their very high water intake on a per body weight basis should be incorporated into any perchlorate risk assessment.

Sincerely,

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National Primary Drinking Water Regulation for Perchlorate

Comment On: EPA-HQ-OW-2018-0780-0001
National Primary Drinking Water Regulations: Perchlorate

Document: EPA-HQ-OW-2018-0780-0243
Comment submitted by Innovative Water Care, LLC

Submitter Information

Organization: Innovative Water Care, LLC

General Comment

In the June 26, 2019 proposed rule for perchlorate, EPA requested comments on the costs and availability of Treatment Technologies as well as potential implementation challenges associated with the proposed perchlorate regulation that the EPA should consider, specifically for small systems. Innovative Water Care, LLC would like to offer the following comments regarding sources of perchlorate contamination and technologies that may be used to avoid perchlorate contamination.

In the EPA-HQ-OW-2018-0780-0127 Perchlorate occurrence and monitoring report, there isnt any breakdown of which systems used chlorine gas and which used sodium hypochlorite solutions, but there is a geographical distribution in Exhibits 16 and 17 that shows a greater occurrence of perchlorate in the southern states where warmer temperatures may be expected to accelerate sodium hypochlorite decomposition and formation of perchlorate. Furthermore, Exhibit A-3 indicates that the median finished water perchlorate concentration (16 ppb) is greater than the median surface (0.248 ppb) and ground (1.5 ppb) water concentrations. These data indicate that the chlorination process may be a contributing factor in perchlorate contamination.

In 2009, the American Water Works Association (AWWA) published the report Hypochlorite- An assessment of factors that influence the formation of perchlorate and other contaminants (AWWA 2009). The document provides data on the effect of storage conditions and other variables on perchlorate formation in sodium hypochlorite solutions and provides guidance on ways to avoid perchlorate formation. In addition to specific storage recommendations, the document provides data on the much lower perchlorate values of calcium hypochlorite.

As stated in the proposed rule, the Safe Drinking Water Act requires that the Agency list the technology, treatment techniques, and other means which the Administrator finds to be feasible for purposes of meeting [the MCL]. The Best Available Technologies (BAT) discussed in Section X of the proposed rule and in EPA-HQ-OW-2018-0780-0111 (Best Available Technologies and Small System Compliance Technologies for Perchlorate in Drinking Water) cover only remedial techniques for removing perchlorate from water. Since chlorination may be a preventable source of perchlorate contamination in drinking water, we believe that the BAT list should include preventative techniques as well as remedial techniques that are feasible for purposes of meeting the proposed MCL values. The guidance provided in AWWA 2009 should be incorporated as Best Available Technologies for prevention of perchlorate contamination. Following is a list of techniques that may be used to minimize perchlorate additions with chlorination:
Dilute stored sodium hypochlorite solutions upon delivery
Store sodium hypochlorite solutions at lower temperatures
Control the pH of stored sodium hypochlorite solutions at pH 11-13, even after dilution
Control the removal of transition metal ions by purchasing filtered hypochlorite solutions and by using low-metal ion concentration feed water for the on-site-generation systems
Use fresh hypochlorite solutions when possible
Make hypochlorite solutions on-site immediately before use by using feed equipment that dissolves solid calcium hypochlorite
Use alternate sources of chlorine where perchlorate contamination is decreased (chlorine gas and solid calcium hypochlorite)
All of these techniques are effective in minimizing perchlorate contamination of drinking water and all of them are appropriate for use by small systems. They meet all of the BAT criteria outlined in Exhibit 1 of EPA-HQ-OW-2018-0780-0111:
High removal efficiency (although the word reduction would be more appropriate here)
History of full-scale operation
General geographic applicability
Compatibility with other treatment processes
Ability to bring all of the water system into compliance
Reasonable cost basis for large and medium systems
These techniques also provide a reasonable cost basis for small systems.

An additional benefit is that these preventative measures do not produce any waste streams such as those that would be created with the currently listed

BAT remediation techniques of ion exchange, biological treatment and reverse osmosis.

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EPA-HQ-OW-2018-0780-0127 Perchlorate occurrence and monitoring report, Office of Water, EPA 816-R-19-003, May 2019.

Environmental Protection Network

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EPN COMMENTS ON PROPOSED PERCHLORATE DRINKING WATER STANDARD

August 26, 2019

The Environmental Protection Network (EPN) is an organization comprised of over 450 EPA alumni volunteering their time to protect the integrity of the U.S. Environmental Protection Agency (EPA), human health and the environment. We harness the expertise of former EPA career staff and confirmation-level appointees to provide an informed and rigorous defense against current Administration efforts to undermine public health and environmental protections.

In the proposed new perchlorate drinking water standard, EPA acknowledges that the lack of robust epidemiology studies makes it very difficult to estimate the likelihood and magnitude of perchlorate's effects on neurodevelopment in fetuses and infants exposed to perchlorate through cord blood, breast milk, and formula. Despite this fact, EPA's proposed perchlorate standard is based on a reference dose (RfD) that includes the lowest possible uncertainty factor of three because the agency maintains all other uncertainty has been eliminated by the use of their Biologically Based Dose Response (BBDR) model. In our comments below, EPN describes the reasons why this uncertainty factor of three does not provide an adequate margin of safety for the perchlorate RfD and must be increased. EPN also comments that the novel approach EPA used to derive a Relative Source Contribution (RSC) for perchlorate must be peer reviewed by external experts before it can be used. Finally, EPN comments on implementation issues in the perchlorate proposal. Based on these concerns, EPN concludes that the proposed perchlorate drinking water standard is not scientifically defensible.

Risk Assessment

EPA derived the proposed Maximum Contaminant Levels (MCLs) using the BBDR model to estimate perchlorate impacts on the thyroid hormones of a pregnant woman at each gestational week from conception to week 16. The model predicts serum thyroid hormone levels of T4 given specific levels of iodine intake, thyroid stimulating hormone (TSH) feedback loop strength, and perchlorate doses. EPA then linked these model predictions of T4 levels to an epidemiology study's measurements of one day's T4 level in a pregnant woman and the intelligence quotient (IQ) of her child. EPA calculated proposed MCLs for perchlorate, which were predicted to produce a 1, 2 or 3% decrease in IQ for a child born to a woman with low iodine intake levels, low T4 levels, and weak TSH feedback strength.

EPN has a number of concerns regarding this approach. First, there were very few data available to calibrate the pharmacokinetic aspects of the model, particularly during the first trimester of pregnancy. Perchlorate and iodide absorption, metabolism and excretion are therefore uncertain. Second, pharmacodynamic data are lacking to calibrate the joint effect of varying perchlorate and iodide serum concentrations on thyroid uptake of iodide and subsequent production of T4 hormone levels from gestation to week 16. Third, the failure to conduct a systematic review of the epidemiology literature undermines the basis for linking the BBDR model results to neurodevelopmental outcomes. It is possible that the 66 studies eliminated from consideration could have provided key information for the overall weight of evidence regarding both serum thyroid function and the relative sensitivity of IQ compared to other neurodevelopmental measures. Even the five studies that EPA considered indicate that IQ is a less sensitive measure than the Mental Development Index and Psychomotor Development Index, which were evaluated in some of those studies.

Finally, EPN notes that there are multiple concerns with the epidemiology study used as the basis of the RfD. According to the American Thyroid Association, the reference range of TSH and T4 in pregnant women varies within the U.S. population and across ethnic groups. Thyroid hormone levels also vary throughout pregnancy, adding to the uncertainty in identifying the level of alteration that may lead to hypothyroidism and fetal effects. The selected epidemiology study involves a non-U.S. population, includes only a one-time measurement of T4 hormone in each pregnant woman, and does not measure iodine intake or perchlorate exposure for any of the women. This lack of critical data impairs the ability of the BBDR model to predict serum T4 hormone levels and the ability to link those hormone levels to an appropriately sensitive neurodevelopmental outcome. It is particularly concerning that EPA has not resolved the critical issues of uncertainty identified previously by the Science Advisory Board, which include the lack of epidemiology data showing a direct association between iodine inhibition and IQ decrement, predictions for lactating mothers with less than 75ug/day iodine intake, and the lack of a standard definition of hypothroxinemia. It appears that EPA is trying to set the precedent that use of a complex model with many variables, which cannot be calibrated, justifies the elimination of uncertainty factors for reference doses. That is not a scientifically defensible policy. EPN concludes that EPA cannot possibly justify the low uncertainty factor of three and should derive new RfDs before proposing a perchlorate drinking water standard.

EPN is also concerned that EPA developed a new methodology to estimate the perchlorate dose that women of childbearing age in the U.S. are getting from food but did not subject this influential analysis to expert external peer review before using it to calculate the proposed MCLs. The new method combines food consumption data for women of childbearing age, from National Health and Nutrition Examination Surveys, with Food and Drug Administration (FDA) data on the perchlorate concentrations in various types of food to calculate each study participant's daily dose of perchlorate. RSCs ranging from 56% to 88% for the three different RfDs were calculated using the 90th percentile bodyweight-adjusted perchlorate consumption based on the second-highest perchlorate concentrations measured by FDA for each type of food. EPA suggests this second-highest concentration is equivalent to a 95th percentile value but did not assign a distribution to the 20 samples available for each type of food. An expert external peer review is needed to evaluate this complex analysis, which is of great interest to women throughout the country who are unknowingly exposed to perchlorate in their food.

Implementation

In addition to our risk assessment concerns, we have the following comments regarding the implementation of the proposed perchlorate drinking water standard.

First, EPN has questions concerning EPA's assumptions about the extent and cost of the initial perchlorate monitoring required by the states and water systems. See Section VIII Monitoring and Compliance Requirements. EPA's estimate significantly overstates the number of water systems that will need to be monitored. It is highly likely that most consecutive systems will not need to to be monitored. States will use their discretion to waive the monitoring requirement where perchlorate is likely not to be found in the water system's source water. EPA must work with states to develop strong implementation guidance to minimize the initial monitoring round, as was done for most of the current regulations implemented in the middle 1990s for inorganic compounds, volatile organic compounds, and synthetic organic compounds. EPN recommends that EPA seek external comments on the high monitoring costs.

Second, EPN has major concerns about the adequacy of EPA's cost-benefit analysis of the proposed regulation. See Section XII Health Risk Reduction Analysis. EPA concluded that for all proposed MCLs, the total annual costs are substantially higher than the proposed benefits.

- The cost-benefit analysis supports the proposed MCL levels of 18, 56, and 90, where the benefits by definition are low since the expected violations to be resolved are very low. A cost-benefit analysis where the costs are much higher than the benefits weakens the validity of the proposal. EPN believes a more stringent standard is justified and that a more stringent value could result in benefits exceeding costs. EPN recommends that EPA withdrawal the current proposal and re-propose a new standard more stringent than the current proposal.
- The cost-benefit analysis itself is very weak. EPA acknowledged that they made many assumptions around the cost-benefit estimates that reduced the benefits estimate and potentially overestimated costs. *On benefits:* They purposely did not consider the obvious benefits of perchlorate treatment in addressing co-occurring violations, such as nitrate. Also, they made no assessment of treatment costs avoided by a water system's decision to switch to a new water source, which is what is happening in both Massachusetts and California to comply with their state perchlorate regulation. *On costs:* They made a very high estimate of the cost of initial monitoring, even though states have wide discretion to waive monitoring requirements for many water systems..

Third, EPN has serious concerns that EPA is including in their perchlorate proposal an option to withdraw from the 2011 regulatory determination and potentially not regulate perchlorate. See Section XV Request for Comment on Potential Regulatory Determination Withdrawal. The proposal states that recent findings suggest that perchlorate does not occur in water systems with a frequency and level of public health concern, and that the perchlorate regulation is no longer a meaningful opportunity for health risk reduction. They also point to EPA's previous determination in 2008 not to regulate perchlorate as precedent, as well as reference other EPA decisions to question regulation (e.g., aldrin) where the occurrence was very low.

EPN has identified serious flaws in the proposal and has serious questions about the scientific defensibility of the EPA perchlorate regulation, the validity of the monitoring, and cost-benefit analysis. EPN strongly recommends that EPA withdrawal the proposal and re-propose a more stringent perchlorate standard with a new cost-benefit analysis. The new proposal should delete the option to withdrawal from the 2011 regulatory determination.

August 26, 2019

U.S. Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington, D.C. 20460

Re: Proposed National Primary Drinking Water Regulation: Perchlorate
Docket No. EPA–HQ–OW–2018–0780

Dear Docket:

The Association of State Drinking Water Administrators (ASDWA) is the independent, nonpartisan, national organization representing the collective interests of the drinking water program administrators in the 50 states, five territories, the District of Columbia, and the Navajo Nation who implement the Safe Drinking Water Act (SDWA) every day to ensure the protection of public health and the economy. ASDWA supports and represents the collective interests of the states, territories, and the Navajo Nation in their administration of national drinking water program requirements within their states or territories. The following ASDWA comments are intended to broadly address the proposed rule, but they do not necessarily reflect the concerns of individual states.

ASDWA appreciates the opportunity to provide comments to EPA on the proposed perchlorate rule, as it is an important rulemaking. This proposal has been over 21 years in the making, with perchlorate being listed on the First Contaminant Candidate List (CCL1) in 1998 and included in the First Unregulated Contaminant Monitoring Rule (UCMR1) in 1999. ASDWA commends EPA for continuing to make regulatory progress throughout those 21 years, and for its focus on developing a better understanding of the challenging health effects data to use in its development of a perchlorate proposal.

ASDWA recognizes that EPA has taken a different regulatory approach for this proposal by proposing a MCLG and MCL of 56 µg/L, as well as MCL options of 18 µg/L and 90 µg/L. EPA used a similar approach for its proposal for the arsenic regulation in 2000, as EPA took comments on four proposed MCLs in that proposal. For perchlorate, EPA has also proposed an option for a negative regulatory determination based on new information indicating perchlorate does not occur with a frequency at levels of public health concern and there may not be a meaningful opportunity for risk reduction through a national drinking water regulation, as required by the Safe Drinking Water Act (SDWA).

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The regulatory development process for perchlorate has been reworked several times since the late 1990s, as EPA proposed a negative regulatory determination in 2008 and then reversed that proposal with a positive regulatory determination in 2011. In the June 26th *Federal Register* (84 FR 30524), EPA published an option for a negative regulatory determination that would reverse the 2011 determination. Since the listing of perchlorate on CCL1 in 1998, two of ASDWA's members (California and Massachusetts) have developed their own state-level perchlorate standard for drinking water. Nevada is also using the interim health advisory as a groundwater cleanup action level for ongoing industrial cleanup actions action in Henderson, Nevada.

In the proposal, EPA did not take into the account the occurrence data (and the resultant treatment costs) for the states (California and Massachusetts) that have developed their own state-level perchlorate standard. One potential concern for future rulemakings based on this approach is, if the Agency continues to exclude states with state-level standards, future rules could be based on a smaller and smaller number of states with the inability to require monitoring or to establish state-level standards.

The ASDWA Board has decided to not take a position on whether to regulate perchlorate or not. The final decision on whether to regulate perchlorate or not is in the "sole judgment of the Administrator" and it is hard to argue one way or the other with that judgment call.

However, if EPA decides to move forward with a final regulation for perchlorate, ASDWA recommends that EPA consider the following items for the final regulation and implementation:

- **Monitoring waivers:** If EPA decides to move forward with a perchlorate regulation, monitoring waivers need to be a significant component of the regulation, as approximately 2/3 of the estimated burden is for monitoring costs. Another significant component of the estimated burden is administrative costs for states, and it should be noted that waiver processes are resource-intensive, and an additional estimate would need to be developed for the increased state administrative burden for waivers. Some states review monitoring waivers by each sampling point, not by each eligible system as calculated in the proposed rule. For those states that review waivers for each sampling point, 8 hours of state review time per eligible system is a gross underestimate. ASDWA recommends that EPA increase its estimate for the states' burden for monitoring waivers. EPA also needs to recognize that any regulatory strategy to reduce the monitoring burden by the water systems through waivers creates additional administrative burden for the states with the review of all the waivers. Additionally, as currently written, 141.23(c)(3)-(6) only requires states to consider previous monitoring history, variation in the results, and system changes in determining waiver eligibility. EPA's occurrence data states that perchlorate is highly mobile and persistent, and exposure can be from man-made sources. Using these sources of exposure in monitoring waivers determinations are not adequately covered in 141.23(c)(3)-(6). EPA would need to update this section of the rules and develop monitoring waiver guidance for states to include potential sources of perchlorate contamination, provide GIS source mapping for potential contaminant locations, when to void a waiver, and how to

address new potential sources of contamination (e.g., new munitions site). Each primacy agency should be able to create their own waiver language that would be approved by the EPA Region. For example, the past cyanide waiver language (based on no industrial uses of cyanide) in 141.23(c)(2) could potentially be modified for perchlorate.

- **Initial monitoring:** If EPA decides to move forward with a perchlorate regulation, then ASDWA recommends four quarters of initial monitoring, to be consistent with the standardized monitoring framework for other inorganic contaminants.
- **Monitoring costs:** As mentioned above, approximately 2/3 of the estimated burden is for monitoring costs. It should be noted that some states conduct the monitoring for water systems, and these costs should be included in the states' burden in the final regulation. More information is needed to determine which states collect and analyze samples for what size systems, but approximately 8-10 states collect and analyze some or all of compliance monitoring samples. EPA should work with ASDWA during the development of the final economic analysis to determine the appropriate split of monitoring costs between the states and the water systems.
- **MCL exceedances:** If EPA decides to move forward with a perchlorate regulation, then the proposed language for addressing MCL exceedances needs to be updated. As proposed, addressing perchlorate MCL exceedances and providing appropriate public notification in a timely manner would be difficult for states to enforce. Under the proposal, if the level of perchlorate exceeds the MCL, a confirmation sample must be collected within 2 weeks of notification of results and compliance with the MCL is determined based on the average of the initial and confirmation samples. However, if the average exceeds the MCL, Tier 1 public notification is required; which is within 24 hours after learning of the violation. Table 2 to 141.201 defines a Tier 1 public notice as "NPDWR violations and situations with significant potential to have serious adverse effects on human health as a result of short-term exposure." Therefore, EPA has proposed an acute MCL for perchlorate that is incongruous with the monitoring requirements of other Tier 1 contaminants. Allowing 2 weeks for an MCL confirmation sample but requiring 24-hour public notice is confusing and ill-advised. EPA would need to update the timeline for confirmation sample collection to follow other Tier 1 MCL exceedances. In addition, EPA did not propose updates to Subpart Q – Public Notification of Drinking Water Violations Table 1 to 141.202—VIOLATION CATEGORIES AND OTHER SITUATIONS REQUIRING A TIER 1 PUBLIC NOTICE restricting states' ability to enforce the Tier 1 requirement. As this is a federal regulation, Table 1 to 141.202 would need to be updated to include perchlorate MCL violations.
- **System Applicability:** Based on the above discussion on 24-hour public notice, it appears to be inconsistent to not have the perchlorate regulation apply to Transient Non-Community (TNC) systems. If EPA decides to move forward with a perchlorate regulation, the EPA should provide justification for not including TNCs.
- **Occurrence data:** Some states have concerns with using the UCMR1 monitoring data that is almost 20 years old. Some states believe this data under-represents national occurrence. Some states have discovered high levels of perchlorate in small systems that were not required to monitor during UCMR1. These small system detections occurred primarily due to aged hypochlorite. Seasonal systems where the hypochlorite

is stored in the off-season also detected high levels of perchlorate. Additionally, many seasonal systems are transient water systems that would not be required to monitor under the proposed rule although an acute MCL level is proposed.

- **Cost burden:** If EPA decides to move forward with a perchlorate regulation, this would be the first regulation with a negative cost-benefit. ASDWA recommends that EPA minimize the negative cost-benefit by evaluating options to reduce both the states' administrative burden (noting our previous comment on states' review of monitoring waivers) and the monitoring costs for states and water systems. As part of its evaluation of the perchlorate proposal, ASDWA asked states to estimate the number of staff hours required to read and understand the rule and to develop a primacy package for perchlorate, as well as a loading percentage for state staff wages. ASDWA received responses from 20 states and the average for both the hours and the loading percentage is in the range of EPA's estimates in its Information Collection Request (ICR) for the proposed perchlorate regulation. However, it should be noted that the primacy package for a potential perchlorate regulation would be relatively simple, as it is a single number for a single contaminant. The state burden for the development and approval of a primacy package (and for training of state staff) for a more complex rule like the Long-Term Revisions to the Lead and Copper Rule (LT-LCR) will be significantly higher.

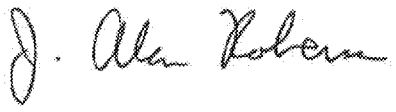
If EPA's final decision is a negative regulatory determination, other states may find there is an opportunity for significant public health protection and determine the need for a state-level standard. Such states would have to follow their own administrative processes for a state-level standard, and EPA should consider helping states with these processes. For example, EPA could help states with exposure assessments, evaluation of analytical methods, and/or treatment technology evaluations.

If EPA's final decision is a negative regulatory determination, then EPA needs to consider the Agency's options for the interim health advisory of 15 µg/L for perchlorate dating back to December 2008. Leaving this health advisory in place after a negative regulatory determination would create confusion for the water systems, primacy agencies and the public. While a health advisory is not a legally enforceable standard, a number is a number to the public. The expected or anticipated actions due to a water system having any water samples over any health advisory have shifted over the past four years, since the publication of health advisories for two cyanobacterial toxins in 2015. The publication of final health advisories in 2016 for perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS) continued to add to the uncertainties for water systems and primacy agencies on what the appropriate actions should be when sample results are over the health advisories.

If EPA's final decision is a negative regulatory determination, then EPA needs to develop additional guidance and/or re-publicize existing technical information on the appropriate management of hypochlorite, as degradation of hypochlorite can contribute to perchlorate exposure. If EPA decides to move forward with a final regulation for perchlorate, ASDWA recommends that EPA discuss the potential exposure from hypochlorite degradation and the appropriate risk management in the final perchlorate regulation.

ASDWA appreciates the opportunity to comment on these important drinking water issues. If you have any questions about these comments or would like the states to provide additional input on the underlying issues, please feel free to email me at aroberson@asdwa.org or give me a call at (703) 812-9507.

Sincerely,



J. Alan Roberson, P.E.
Executive Director
Association of State Drinking Water Administrators (ASDWA)

cc: David Ross – EPA OW
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OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT

Public Health Goal

Perchlorate in Drinking Water

February 2015

Pesticide and Environmental Toxicology Branch
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency

Public Health Goal for

PERCHLORATE

in Drinking Water

Prepared by

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February 2015

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PREFACE

This Public Health Goal (PHG) technical support document provides information on health effects from perchlorate in drinking water. PHGs are developed for chemical contaminants based on the best available toxicological data in the scientific literature. The PHG documents and the analyses contained in them provide estimates of the levels of contaminants in drinking water that would pose no significant health risk to individuals consuming the water on a daily basis over a lifetime. The PHG is a drinking water goal only; therefore, this document does not evaluate the safe levels of perchlorate in foods or other sources.

The California Safe Drinking Water Act of 1996 (Health and Safety Code, Section 116365) requires the Office of Environmental Health Hazard Assessment (OEHHA) to perform risk assessments and publish PHGs for contaminants in drinking water based exclusively on public health considerations. Section 116365 specifies that the PHG is to be based exclusively on public health considerations without regard to cost impacts. The Act requires that PHGs be set in accordance with the following criteria:

1. PHGs for acutely toxic substances shall be set at levels at which no known or anticipated adverse effects on health will occur, with an adequate margin of safety.

2. PHGs for carcinogens or other substances that can cause chronic disease shall be based upon currently available data and shall be set at levels that OEHHA has determined do not pose any significant risk to health.

3. To the extent the information is available, OEHHA shall consider possible synergistic effects resulting from exposure to two or more contaminants.

4. OEHHA shall consider the existence of groups in the population that are more susceptible to adverse effects of the contaminants than a normal healthy adult.

5. OEHHA shall consider the contaminant exposure and body burden levels that alter physiological function or structure in a manner that may significantly increase the risk of illness.

6. In cases of insufficient data to determine a level of no anticipated risk, OEHHA shall set the PHG at a level that is protective of public health with an adequate margin of safety.

7. In cases where scientific evidence demonstrates that a safe dose-response threshold for a contaminant exists, then the PHG should be set at that threshold.

8. The PHG may be set at zero if necessary to satisfy the requirements listed above.

9. OEHHA shall consider exposure to contaminants in media other than drinking water, including food and air and the resulting body burden.

10. PHGs published by OEHHA shall be reviewed every five years and revised as necessary based on the availability of new scientific data.

PHGs published by OEHHA are for use by the State Water Resources Control Board (SWRCB) in establishing primary drinking water standards (State Maximum Contaminant Levels, or MCLs). Whereas PHGs are to be based solely on scientific and public health considerations without regard to economic cost considerations, drinking water standards adopted by SWRCB are to consider economic factors and technological feasibility. Each standard adopted shall be set at a level that is as close as feasible to the corresponding PHG, placing emphasis on the protection of public health. PHGs established by OEHHA are not regulatory in nature and represent only non-mandatory goals. By federal law, MCLs established by SWRCB must be at least as stringent as the federal MCL if one exists.

In July 2014, responsibility for the state's drinking water regulatory program was transferred to SWRCB from the Calfornia Department of Public Health. References in this document to drinking water monitoring and regulation may cite either or both entities as appropriate.

Additional information on PHGs can be obtained at the OEHHA web site at www.oehha.ca.gov.

CONTENTS

PUBLIC HEALTH GOAL FOR PERCHLORATE IN DRINKING WATER

SUMMARY

The Office of Environmental Health Hazard Assessment (OEHHA) is publishing a Public Health Goal (PHG) of 1 part per billion (ppb) (equivalent to 1 microgram per liter [µg/L]) for perchlorate in drinking water. Perchlorate is an oxidizing chemical used in a variety of industrial processes. Perchlorate can occur in the environment either through industrial contamination or from natural sources. Perchlorate exposure in the U.S. is ubiquitous, mostly from ingestion of perchlorate in contaminated food or water. In a survey involving an essentially random sample of people from the U.S., perchlorate was detected in the urine of every one of the 2,820 subjects tested (Blount *et al.,* 2006).

Health Impacts from Perchlorate

For this PHG, OEHHA used decreased uptake of iodide by the thyroid gland as the key biochemical event for assessing the risks due to perchlorate toxicity. The primary action of perchlorate in humans is inhibition of iodide uptake into the thyroid gland. The function of the thyroid gland is the production of thyroid hormone. Iodide is a key component in the structure of thyroid hormone, and by blocking its uptake into the thyroid, perchlorate can potentially cause decreased production of this hormone.

Thyroid hormone is necessary for a variety of basic human physiologic functions, including controlling basal metabolic rates; protein, carbohydrate, and fat metabolism; protein synthesis; proper differentiation and development of cells, including neuronal cells; and the cognitive and physical development of the fetus, infant, and child. Evidence suggests that even small decreases in thyroid hormone levels may be associated with significant adverse effects, including altered cognitive development in children and increased cardiovascular risk factors in adults. Importantly, these changes have been seen at thyroid hormone levels that are within what have been traditionally defined as normal reference ranges, and have occurred in people without any other evidence of overt thyroid disease. These findings suggest that small changes in thyroid hormone levels may be associated with some increased risk of thyroid-related adverse outcomes.

There is a continuum in the possible health effects from perchlorate exposure resulting from its effects on the thyroid, and some susceptible groups or individuals may have perchlorate-related effects at exposures that are lower than those causing similar effects in healthy individuals. For fetuses, infants and children, there is the potential for abnormal growth and development. Of particular concern are effects on brain development. Decreases in thyroid hormone production in infants are related to decreases in IQ. Much of the knowledge on the potential effects of perchlorate comes from extensive data on iodine deficiency in humans.

OEHHA considers effects on thyroid hormone production and subsequent changes to be adverse. Iodide uptake inhibition is the key event that leads to other possible effects from perchlorate exposure. Prevention of iodide uptake inhibition prevents progression to the adverse health effects of perchlorate. The inhibition of iodide uptake by perchlorate has been clearly documented in humans. The National Academy of Sciences (NAS, 2005) deemed "inhibition of iodide uptake by the thyroid as the basis of the perchlorate risk assessment to be the most health-protective and scientifically valid approach." OEHHA agrees with this approach and used it in developing its original 2004 PHG for perchlorate.

The Greer *et al.* (2002) study was used to characterize perchlorate's inhibition of iodide uptake for both the current PHG and the 2004 PHG. It might be argued that the magnitudes of the effects seen in the Greer *et al.* (2002) study were relatively small, and might not be noticeable in otherwise healthy individuals. However, this ignores the impact of these effects on a population basis. Any downward shift in the mean level of the thyroid hormone T4 in a population could increase the number of people who fall into the range of T4 values that are associated with high risks of either subtle or overt thyroid-related disease and toxicity (Miller *et al.,* 2009).

The perchlorate PHG of 1 ppb is intended to help prevent any perchlorate-related decrease in iodide uptake by the thyroid that could lead to decreased thyroid hormone production and that could disrupt the important functions of this hormone.

Estimating the Acceptable Daily Dose for Perchlorate

The PHG was derived by first calculating an Acceptable Daily Dose (ADD). This is consistent with the approach taken by the NAS (2005). The ADD is defined as the estimated maximum daily dose that can be consumed by humans for an entire lifetime without toxic effects, and is similar in definition to the reference dose (RfD) used by the U.S. Environmental Protection Agency (U.S. EPA). The ADD for perchlorate was estimated using data from the human study by Greer *et al.* (2002). This is the same study used in developing OEHHA's 2004 perchlorate PHG, and by the NAS (2005) in developing its perchlorate reference dose.

Health Value from the Greer *et al.* Study

In the Greer *et al.* (2002) study, a daily oral dose of perchlorate was administered to groups of male and female volunteers for 14 days at doses of 0.007, 0.02, 0.1, or 0.5 mg/kg-day. Reductions in iodide uptake by the thyroid gland were seen at all four dose levels, with statistically significant reductions at the highest three doses. These results were plotted and dose-response relationships fitted to estimate the dose of perchlorate likely to cause a five percent decrease in iodide uptake. This dose was defined as the Benchmark Dose (BMD), and its lower 95 percent confidence limit was defined as the BMDL. This is the same method and data set used to establish the 2004 perchlorate PHG, and the BMD of 6.8 µg/kg-day and BMDL of 3.7 µg/kg-day are the same. The units µg/kg-day refer to micrograms (µg) of perchlorate ingested in one day per kilogram (kg) of body weight.

OEHHA used the BMD approach rather than the no-observed-effect level (NOEL) approach for the following reasons. OEHHA, like U.S. EPA, has chosen to use the BMD approach as the standard method in dose calculations, provided there are sufficient data to do so. As the U.S. EPA (2012, p. viii) notes, the BMD approach "involves dose-response modeling to obtain BMDs, i.e., dose levels corresponding to specific response levels near the low end of the observable range of the data, incorporates and conveys more information than the [NOAEL; no-observed-adverse-effect level] or [LOAEL; lowest-observed-adverse-effect level] process traditionally used for noncancer health effects." The NAS (2009, p. 129) in its review of U.S. EPA risk assessment practices similarly has recognized this as a refinement that makes better use of the dose-response evidence available than do calculations based on NOAELs.

The NOEL approach depends heavily on a single chosen dose level used in a study, and how closely it is placed relative to the next highest dose. The NOEL approach treats small and large studies the same, even though small studies, with their limited number of subjects, are less likely than large studies to find health effects at any given dose. In this case, the small group sizes in the Greer *et al.* (2002) study make it more difficult to detect an effect. For these reasons reliability of the NOEL approach can vary depending on the size of the study. In contrast, the BMD approach provides a systematic method for calculating a dose at a low specific effect level. The BMD approach uses all the dose-response evidence in the study, incorporates the shape of the dose-response curve, and takes into account the number of subjects in the study, thus providing a more reliable calculation. The advantages of using the BMD approach for this PHG are particularly important given the limited number of subjects that participated in the Greer *et al.* (2002) study.

Sensitive Populations

In the next step, the ADD of 0.37 µg/kg-day was calculated by dividing the BMDL by an uncertainty factor of 10. The NAS also used a 10-fold uncertainty factor in

developing its perchlorate reference dose (NAS, 2005). This uncertainty factor reflects the varying susceptibility of humans to perchlorate and was used because the Greer *et al.* (2002) study involved only healthy adult volunteers.

A fairly extensive body of evidence suggests that certain population subgroups may be much more susceptible to the effects of perchlorate than healthy adults. In reviewing the literature, OEHHA identified several reasons why infants, especially those that are born prematurely, are likely to have increased susceptibility to perchlorate. We also identified several other groups as likely having increased susceptibility, including fetuses, pregnant women, those with low intakes of iodine, and those exposed to other chemicals in food and water that, like perchlorate, also block iodide uptake into the thyroid.

The major change in the current PHG calculation relates to the updated information on infants as a sensitive population. OEHHA's review and updating of the perchlorate PHG considered the data from several human studies published after the 2004 PHG and the 2005 NAS review. These studies provided qualitative support for recognizing that infants are likely to be significantly more susceptible to perchlorate than healthy adults. Evidence for this includes the following:

1. New data suggest that many infants may not be receiving adequate iodine in their diets. In a study of nursing mothers in Boston, 47 percent of breast milk samples did not contain enough iodine to meet the infant iodine intake recommended by the Institute of Medicine (Pearce *et al.,* 2007). Perchlorate-related toxicity is likely to be greater in infants who are already deficient in iodine.
2. OEHHA's analysis of data from studies conducted in California and elsewhere provide evidence that thyroid hormone levels in infants were adversely affected by perchlorate at exposure levels that were much lower than the levels shown to cause no effects in healthy adults (Kelsh *et al.,* 2003; Brechner *et al.*, 2000; Buffler *et al.,* 2006; Steinmaus *et al.*, 2010; Li *et al.,* 2000a; Crump *et al.,* 2000).
3. Young infants have low stores of thyroid hormone (less than one day's worth, compared to several weeks' worth in adults) (van den Hove *et al.*, 1999). Because of these low stores, infants may be less able to tolerate transient periods of decreased iodide uptake and decreased thyroid hormone production compared to adults.
4. Human data suggest that perchlorate can interact with other contaminants to produce a greater effect than that caused by perchlorate alone (Blount *et al.*, 2006; Steinmaus *et al.*, 2007), and infants are exposed to these same contaminants.

In the 2004 PHG, an uncertainty factor of 10 was applied to address all sensitive groups (pregnant women, lactating women, thyroid compromised adults) except infants, where an uncertainty factor of 3 was used. However, given the evidence discussed above, the extent and ways infants are likely to be more susceptible to

perchlorate than healthy adults, and the fact that the Greer *et al.* (2002) study included only healthy adults, OEHHA has increased the uncertainty factor applied to infants from the factor of 3 used in the 2004 PHG to a factor of 10 in this updated PHG. This was one factor that resulted in the lowering of the updated PHG. The other factor driving the change in the PHG value is the use of updated drinking water intake rates for infants, described below.

Calculating the PHG

The ADD was then used to develop the PHG in the following two steps. First, the ADD was converted into an acceptable drinking water perchlorate concentration (in units of µg of perchlorate per liter (L) of drinking water). This was done by dividing the ADD by a drinking water intake rate expressed in terms of liters of water consumed per day per kilogram of body weight. The second step involves accounting for perchlorate intake from sources other than drinking water.

Water Consumption by Infants

The water consumption rate by infants is one of the factors that influence the final PHG. The recent analysis by OEHHA (2012) of data available from a large survey of food and beverage intake conducted by the U.S. Department of Agriculture shows that drinking water intakes per kilogram of body weight are higher in infants than previously thought. This means that infants are likely to have greater perchlorate exposure per kilogram of body weight for a given concentration of perchlorate in drinking water than was estimated in the 2004 PHG.

OEHHA used its new analysis and chose the 95th percentile drinking water intake rate instead of an average rate in order to protect the infant population, and not just those with average drinking water consumption. Infants who drink more water will have a greater exposure to perchlorate and thus may be at greater risk. In this case the bottle-fed infant will have the greatest intake of water and exposure to water contaminants.

The 95th percentile value of 0.237 L/kg-day for drinking water intake per body weight for infants aged 0-6 months (OEHHA, 2012) was used in the PHG calculations. For comparison, U.S. EPA (2009) typically assumes that infants and children drink 1 liter (L) per day and that they weigh 10 kilograms, that is 0.1 L/kg-day. Using the U.S. EPA value would result in a PHG of 2.7 ppb instead of 1 ppb.

Relative Source Contribution: Addressing Perchlorate Exposure from Other Sources

In the second step of the PHG calculation, an adjustment was made to account for perchlorate intake from sources other than drinking water. Because the ADD is the acceptable daily dose for all sources of perchlorate intake combined (i.e.,

food plus water), estimated intakes from food must be accounted for when developing a PHG for drinking water. This is a standard approach for developing drinking water criteria and is also required under Health and Safety Code Section 116365 (c)(1)(C)(iv). In OEHHA's review, it was determined that food was the only other significant source of perchlorate exposure in the large majority of people. Intake from food is accounted for by multiplying the ADD by the relative source contribution (RSC), defined as the fraction of the ADD (which incorporates perchlorate from food plus water) expected to come from water. Since infants were identified as a susceptible group, the amount of perchlorate expected to come from food was estimated using the median perchlorate levels in powdered infant formula reconstituted with perchlorate-free water (Schier *et al.*, 2010).

Based on these data, OEHHA calculated a RSC of 0.73. These two steps were used to develop an updated health-protective concentration (C) based on the following calculations: C = ADD × RSC ÷ drinking water rate = 0.37 µg/kg-day × 0.73 ÷ 0.237 L/kg-day = 1 µg/L, that is 1 ppb. Thus, the PHG for perchlorate in drinking water is 1 ppb.

Comparison with Other Agencies

In 2004 a PHG of 6 ppb was set for perchlorate, and the California Maximum Contaminant Level (MCL) for perchlorate was subsequently set at 6 ppb (Ting *et al.*, 2006). Currently, there is no federal MCL for perchlorate. The current OEHHA PHG of 1 ppb updates the PHG of 6 ppb set in 2004.

PHGs published by OEHHA are for use by the State Water Resources Control Board (SWRCB) in establishing primary drinking water standards, that is, the California MCLs. In developing the PHG for perchlorate, OEHHA's approach follows that used by the NAS (2005) to develop its reference dose in several key areas:

1. Both OEHHA and NAS identified the Greer *et al.* (2002) human study as the critical study for evaluating the effects of perchlorate.
2. Both OEHHA and NAS chose iodide uptake inhibition in the Greer *et al.* (2002) study as the key effect on which to base their calculations.
3. Both OEHHA and NAS noted that the subjects in the Greer *et al.* (2002) study were healthy adults and concluded that some people may be more susceptible to perchlorate than these healthy adult subjects. For this reason, both OEHHA and NAS applied an uncertainty factor of 10 to calculate a dose that would address inter-individual variability among humans and be protective of those who are likely to be sensitive to the effects of perchlorate.
4. Both OEHHA and NAS identified the same populations likely to be more sensitive to perchlorate exposure: fetuses, preterm newborns, infants, developing children, pregnant women, people who have compromised

thyroid function resulting from conditions that reduce thyroid hormone production, and people who are iodine-deficient.

There is only one substantive difference between the OEHHA and NAS analyses. The NAS used the no-observed-effect level (NOEL) approach. They determined that the NOEL was 0.007 mg/kg-day, the highest dose in the Greer *et al*. (2002) study that was not associated with a statistically significant response. OEHHA used the Benchmark Dose (BMD) approach and calculated a point of departure of 0.0037 mg/kg-day. As discussed above, the BMD method is a statistical method that is now widely recognized as a better approach because it incorporates more dose-response information from the study than the NOEL method (NAS, 2009; U.S. EPA, 2012).

From the NOEL, the NAS calculated a reference dose of 0.0007 mg/kg-day (the NOEL divided by the uncertainty factor of 10). OEHHA similarly calculated an ADD of 0.00037 mg/kg-day (the BMD-derived point of departure divided by the same10-fold uncertainty factor). Thus the two approaches differ by less than a factor of 2. The NAS did not take the next step to calculate an acceptable drinking water level for perchlorate.

Conclusion

In conclusion, the primary toxic mechanism of perchlorate is a reduction in iodide uptake into the thyroid gland. If severe enough, this can lead to reduced thyroid hormone production. Adequate supplies of thyroid hormone are vital for a variety of physiologic processes, and even small reductions in thyroid hormone have been associated with increased cardiovascular disease risk factors, abnormal fetal brain development, and altered childhood cognition. The purpose of this updated PHG of 1 ppb is to identify a level of perchlorate in drinking water that prevents perchlorate-related reductions in thyroidal iodide uptake and subsequent decreases in thyroid hormone production that may be associated with any of these adverse health effects.

1. INTRODUCTION

Purpose

The purpose of this document is to evaluate current scientific information on perchlorate in order to update the health-protective concentration estimate, or Public Health Goal (PHG), for perchlorate in drinking water. PHGs are based on a comprehensive analysis of information on the toxicology of drinking water contaminants, and are based solely on protection of public health without regard to cost impacts or other factors. PHGs for carcinogens are set at a *de minimis* risk level of one in a million (10^{-6}), assuming a lifetime of exposure to the chemical in the drinking water. PHGs for noncarcinogens are based on levels estimated to be without risk of any adverse effects for exposures up to a lifetime, to the general population as well as any significant identifiable sensitive subpopulations.

Perchlorate is a ubiquitous environmental contaminant. It is apparently formed by sunlight or lightning interacting with oxygen and chlorine in the atmosphere, and falls to the earth in rain (Dasgupta *et al.*, 2005; Mohan, 2010). Plants can accumulate perchlorate from the water they take up. Perchlorate is also released to the environment from its use in highway flares, fireworks and other explosives, and rocket fuel. People are primarily exposed to perchlorate through consumption of food and water.

Exposure to perchlorate may cause harmful health effects due to its competition with iodide for uptake into the thyroid gland. Iodide is used by the thyroid gland to make the thyroid hormones thyroxine and triiodothyronine (also known as T4 and T3). Decreased uptake of iodide can decrease production of thyroid hormone and impair normal metabolism and growth. Several other chemicals that people are commonly exposed to, such as nitrate, thiocyanate, and bromide, can also compete with iodide for uptake into the thyroid. Maintenance of normal production of thyroid hormone depends on the availability of iodide, obtained mostly from the diet, as well as the combined effects of the various competitors for iodide uptake.

This document represents an update of an earlier health risk assessment of perchlorate conducted by OEHHA that resulted in the publication of a PHG in 2004. This revision takes into account information which suggests that infants can be especially susceptible to perchlorate, along with pregnant women and their fetuses and those with iodine deficiencies. This revision also incorporates the higher drinking water consumption values described by OEHHA (2012) to be more protective of the entire population.

Chemical Profile

Chemical Identity

Perchlorate (ClO_4^-) is the most oxygenated member of a series of four anions made up of chlorine and oxygen. The anion has a charge of negative one, and can form an acid or a salt in combination with H^+ or another cation such as sodium, potassium or ammonium. Perchlorate salts are ionic, and dissociate completely when dissolved in water. This risk assessment is for the perchlorate anion in water, regardless of the cation.

Physical and Chemical Properties

Ammonium perchlorate (NH_4ClO_4), the salt used as an oxidizer in rocket propellants, is a white, crystalline solid. As ammonium perchlorate is the major source of most of the perchlorate that has been detected in drinking water sources in California and Nevada (U.S. EPA, 1998a), it is used as the model compound to illustrate some of the physical and chemical properties of perchlorate salts (Table 1).

Table 1. Physical and Chemical Properties of Ammonium Perchlorate (from HSDB, 2010)

Property	Value or Information
Molecular Weight	117.49
Color/Physical State	White orthorhombic crystals
Melting Point	130°C, starts to decompose at 439°C
Solubility in water	200 g/L at 25°C
Solubility in organic solvents	Soluble in methanol, slightly soluble in ethanol and acetone, almost insoluble in ethyl acetate, ether
Density	1.95 g/cm^3

Production and Uses

Ammonium perchlorate is used as an oxidizer in solid rocket propellant. Sodium perchlorate is used in slurry explosives, and potassium perchlorate is used in road flares and air bag inflation systems. The manufacture of perchlorate salts begins with the electrolysis of brine (sodium chloride in water) to first form sodium chlorate ($NaClO_3$) and then sodium perchlorate ($NaClO_4$). This is reacted with ammonium chloride to form ammonium perchlorate (NH_4ClO_4) and sodium chloride. The solution is cooled, and the ammonium perchlorate crystals are dried and packaged.

Ammonium perchlorate is mixed with metallic aluminum in a synthetic rubber base to make rocket fuel. This type of fuel is used in the Minuteman missile, which has been deployed in the United States since 1961. Perchlorate salts are also used as a component of air bag inflators, in nuclear reactors and electronic tubes, as additives in lubricating oils, in tanning and finishing leather, as a mordant for fabrics and dyes, and in electroplating, aluminum refining, rubber manufacture, and the production of paints and enamels (U.S. EPA, 2002).

Perchlorate has been used as a growth promoter in leguminous plants (Verteletskaya *et al.*, 1974; as cited in Von Burg, 1995), livestock (sheep and cattle) and poultry (Yakimenko *et al.*, 1981; as cited in Von Burg, 1995). Research from the former Soviet Union indicated that weight gains in livestock of 3 to 31 percent were obtained by addition of ammonium perchlorate to the feed. Feed expenditure was also reduced 7-18 percent. The optimum dose was estimated to be 2-5 mg/kg (Grayson, 1978). Weight gains in livestock may be secondary to hypothyroidism and decreased metabolic rates. This is most likely a non-nutritive effect associated with the inhibition of thyroid hormone production and subsequent hypothyroidism.

Perchlorate has no known nutritional use. In 1952, investigators observed that perchlorate displaces iodide from the rat thyroid (Wyngaarden *et al.*, 1952). Since then perchlorate has been widely used in laboratory studies on the thyroid to block entry of iodide into the thyroid, or to cause discharge of noncovalently bound iodide previously accumulated in the thyroid (Wolff, 1998).

Environmental Occurrence and Human Exposure

Perchlorate can apparently be formed by sunlight or lightning interacting with oxygen and chlorine in the atmosphere (Dasgupta *et al.*, 2005; Mohan, 2010). As perchlorate falls to the earth in rain, it can distribute at low levels throughout the environment, in both soil and water. Plants can accumulate perchlorate from the water they take up (U.S. EPA, 2001a; Jackson *et al.*, 2005; Sanchez *et al.*, 2005 a,b, 2008).

Perchlorate is also released to the environment from its use in highway flares, fireworks and other explosives, and rocket fuel. Perchlorate salts have been widely used as an oxidizer in solid propellants for rockets and missiles since the mid-1940s. Because of its finite shelf life, the propellant containing perchlorate has been periodically washed out of the United States' missile and rocket inventory to be replaced with a fresh supply (U.S. EPA, 1998a). As a consequence of this practice, large volumes of perchlorate have been disposed of since the 1950s. Some of this has leached into soil, and into aquifers used for drinking water. Perchlorate is highly mobile in aqueous systems and can persist for many decades under typical ground and surface water conditions (U.S. EPA, 1998a).

Air

Some unreacted perchlorate is occasionally released to the atmosphere during the launch of solid fuel rockets. Releases have also occurred as a consequence of open burning and detonation of old rocket fuel or surplus materials. No data were found on levels of perchlorate in ambient air.

Perchlorate dust can also be suspended in air, and can be inhaled by individuals working in areas where perchlorate is manufactured (Lamm *et al.*, 1999).

Soil

As a result of past disposal practices, including replacement of rocket fuel supplies noted above, soil and groundwater near the facilities that had been engaged in rocket fuel manufacturing and disposal are contaminated (U.S. EPA, 1998a). Releases to soil might also have occurred because of the past open burning and open detonation of perchlorate-containing material. Another way in which soil can become contaminated is by irrigation with perchlorate-contaminated water.

A report by TRC Environmental Corporation (1998) raised the concern that some chemical fertilizers may be contaminated with perchlorate. In the past, some fertilizers derived from Chilean caliche (a natural perchlorate source) were found to be contaminated with perchlorate. Since this discovery, the producer of Chilean caliche has changed its practice and eliminated the perchlorate contamination. U.S. EPA (2001b) tested a variety of fertilizers collected from representative sites around the nation and did not find perchlorate contamination to be a problem.

Water

Drinking water sources have become contaminated with perchlorate as a consequence of soil pollution in areas where solid rocket fuel has been manufactured, used, or disposed of. Perchlorate salts are soluble in water and once dissolved, perchlorate ion can persist in surface and ground waters for several decades (U.S. EPA, 1998a).

Until March 1997, the detection limit for perchlorate in water was rather high, at 400 µg/L (ppb). In March 1997, California Department of Health Services (DHS), now the California Department of Public Health (DPH), developed a more sensitive analytical procedure, using ion chromatography, and achieved a detection limit in the 4-5 ppb range (DHS, 2000). Shortly thereafter, the new technology was adopted by a number of commercial laboratories. U.S. EPA Method 314.0 (Federal Register, 2000) now exists for analysis of perchlorate in water and has a detection limit as low as 0.5 ppb.

Since March 1997, California DPH (and now SWRCB) has reported measurements of perchlorate concentrations in thousands of drinking water sources and wells throughout the state. Between 2010 and 2013, perchlorate concentrations above 4 ppb were reported in 248 drinking water sources in California (Table 2).

Urbansky *et al.* (2000) analyzed samples of eight domestic brands and eight imported brands of bottled water and did not find perchlorate (with a detection limit of 5 ppb) in any of the samples.

Blount *et al.* (2010) measured perchlorate concentrations in tap water samples collected from 3,262 subjects from the 2005-6 United States National Health and Nutrition Examination Survey (NHANES), and reported a geometric mean of 0.714 µg/L (95% confidence interval (CI), 0.551-0.998 µg/L). Using these measurements, and 24-hour recall data on tap water consumption, the authors estimated a median perchlorate intake of 9.11 ng/kg-day from tap water for U.S. men and women over age 12. The relevance of these findings to California, especially to those areas with documented perchlorate contamination, is unknown, and estimated intakes in potentially susceptible groups such as infants were not reported.

Food

Plants take up perchlorate from water, and probably also from fertilizers which contain perchlorate (U.S. EPA, 2001a; Trumpolt *et al.*, 2005). In a greenhouse study, U.S. EPA researchers watered lettuce plants with one of five different concentrations of perchlorate (0.1, 0.5, 1.0, 5.0, and 10.0 µg/mL) for a period of 90 days following planting. They found perchlorate levels rose steadily over the first 50-60 days, and then generally leveled off. The amount of perchlorate detected in the leaves correlated with the water concentration. At about 50 days into the study, the lettuce irrigated with 10.0 µg/mL (ppm) perchlorate had a perchlorate content of about 300 µg/g on a wet weight basis (U.S. EPA, 2002).

Table 2. Reported Perchlorate Detections in California 2010-2013 (from SWRCB, 2014) [a, b]

	Peak ≥ 4 µg/L		Peak ≥ 6 µg/L		
County	No. of Sources	No. of Systems	No. of Sources	No. of Systems	Highest Peak (µg/L)
Contra Costa	1	1	1	1	7.9
Fresno	1	1	-	-	4.5
Kern	2	2	1	1	14
Los Angeles	98	31	68	21	108
Monterey	1	1	-	-	4.8
Orange	11	7	3	2	9
Riverside	49	8	38	8	68
Sacramento	2	1	2	1	13
San Bernardino	57	19	37	16	94
San Diego	10	2	8	2	9.9
Santa Barbara	1	1	-	-	4.6
Santa Clara	5	4	3	3	10
Sutter	3	3	1	1	10
Tulare	6	3	5	3	20
Ventura	1	1	-	-	5.2
TOTAL	248	85	167	59	-

[a] Data for perchlorate were extracted from the water quality monitoring database (http://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/EDTlibrary.shtml).

[b] Where raw and treated samples or other results indicate more than one sampling point for the same source, they are counted as coming from a single source. All detections greater than the detection limit for purposes of reporting (DLR), however, are available here: http://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/Documents/Perchlorate/perchloratedetects2010-2013forweb.xls.

Scientists at Texas Tech University (Lubbock, Texas) developed sensitive methods for assaying perchlorate in biological samples and reported perchlorate accumulation in a variety of crops as well as in animals, trees and aquatic plants (Smith *et al.,* 2001, 2004; Tan *et al*., 2004; Yu *et al*., 2004; Jackson *et al*., 2005). Concentration factors well over 100-fold, compared to the concentration in the water, were reported in some plants. Sanchez *et al*. (2005a,b) showed that perchlorate accumulated in lettuce and other leafy vegetables when grown with

Colorado River water contaminated with perchlorate at low ppb levels. Later studies by the same workers documented uptake in a wider variety of crops (Sanchez *et al.*, 2006, 2008).

In 2004-5, the U.S. Food and Drug Administration (U.S. FDA) measured perchlorate concentrations in many different types of foods. Results for 27 foods and beverages collected from areas where perchlorate was known to contaminate drinking water were reported (U.S. FDA, 2009). Multiple assays were conducted on each product, for a total of 775 results. Reported average values ranged from 0.15 ppb (µg/L) in potatoes (set at one-half the limit of detection, since all values were non-detect) to 92.4 ppb in "greens." Shrimp was second-highest, at 19.83 ppb. Cow's milk averaged 5.81 ppb.

Using food consumption estimates from the U.S. Department of Agriculture's Continuing Survey of Food Intake by Individuals (CSFII 1994-96 and 1998 Supplemental Children's Survey), U.S. FDA estimated dietary perchlorate consumption for various population groups. Mean perchlorate intake of persons aged 2 years and above was estimated to be 0.053 µg/kg-day. The estimated mean intakes for children aged 2-5 years, and for females aged 15-45 years, were 0.17 and 0.037 µg/kg-day, respectively. The estimated 90th percentile intakes were 0.12 µg/kg-day for all people aged 2 years and older; 0.34 µg/kg-day for children aged 2-5 years; and 0.074 µg/kg-day for females aged 15-45 years.

More recently, U.S. FDA has included perchlorate analysis in its Total Diet Study, which involves a periodic analysis of 285 foods selected to be representative of the total U.S. diet. As reported by Murray *et al.* (2008), food products were sampled in 2005-2006. Estimates of perchlorate intake were made using the CSFII data as described above. Upper and lower bound consumption estimates for various population groups are shown in Table 3. These perchlorate exposure estimates tend to be higher than the earlier FDA estimates, but they cover more foods.

There are concerns that breast milk may represent an exposure pathway for infants. In a study reported by Yu (2000), groups of female rats were treated with perchlorate in drinking water at 0, 0.01, 0.1, 1, and 10 mg/kg-day throughout gestation and lactation. On postnatal day 10, the rats were milked. Yu found the levels of perchlorate in milk were about twice as high as the corresponding levels in maternal serum across all doses, suggesting that perchlorate is actively sequestered into milk. Clewell *et al.* (2003) reported that perchlorate was indeed transferred to the pup through suckling as perchlorate was detected in milk, as well as in the neonate serum, gastrointestinal contents, and skin.

Human mammary gland during lactation has been shown to express the sodium-iodide symporter (NIS), the protein responsible for moving iodide into the thyroid and, in this case, into breast milk. The mammary gland may have the capability to actively secrete perchlorate into the breast milk (Vayre *et al.*, 1999; Tazebay *et*

al., 2000). Another concern is that iodide in breast milk is necessary for thyroid hormone synthesis by the newborn. Perchlorate inhibits the NIS in the lactating mammary gland and can interfere with the secretion of iodide into breast milk. This reduction in iodide transfer has been seen in cows and goats (Howard *et al.*, 1996; Lengemann, 1973; Mountford *et al.*, 1987).

Rice *et al.* (2007) analyzed the relationship between perchlorate in feed given to dairy cows and the resulting levels in milk. They reported that significant perchlorate exposures occurred from perchlorate in corn silage, alfalfa, and grass. Sanchez *et al.* (2008) also showed that perchlorate in alfalfa makes a major contribution to perchlorate levels in the milk of dairy cows.

Table 3. Estimated Perchlorate Intakes from U.S. FDA's Total Dietary Survey: Results for 2005–2006 (as reported in U.S. EPA, 2008b)

Population group		Perchlorate intake from food µg/kg-day	
		Lower-bound	Upper-bound
Infants	6-11 mo.	0.26	0.29
Children	2 yr.	0.35	0.39
Children	6 yr.	0.25	0.28
Children	10 yr.	0.17	0.20
Teenage Girls	14-16 yr.	0.09	0.11
Teenage Boys	14-16 yr.	0.12	0.14
Women	25-30 yr.	0.09	0.11
Men	25-30 yr.	0.08	0.11
Women	40-45 yr.	0.09	0.11
Men	40-45 yr.	0.09	0.11
Women	60-65 yr.	0.09	0.10
Men	60-65 yr.	0.09	0.11
Women	70+ yr.	0.09	0.11
Men	70+ yr.	0.11	0.12

Kirk *et al.* (2005) analyzed perchlorate concentrations in 47 different samples of dairy milk from 11 different states and 36 human milk samples from lactating women from 18 different states. Detectable levels of perchlorate were found in all but one of the samples tested. The mean perchlorate concentration in the breast milk samples was 10.5 µg/L. Iodine concentrations in milk were inversely correlated with perchlorate concentrations, but only in the six samples with perchlorate concentrations above 10 µg/L (coefficient of variation (R^2) > 0.9). In a later study, Kirk *et al.* (2007) measured perchlorate levels in 10 lactating women in six breast milk samples per day per woman for three days. The mean

perchlorate concentration was 5.8 µg/L (standard deviation (SD) ± 6.2 µg/L). Considerable variability was seen both among and between individuals.

Pearce *et al.* (2007) measured breast milk perchlorate levels in 49 women from the Boston area and in 17 different infant formulas. Perchlorate was detectable in all 49 breast milk samples tested and in all 17 infant formula samples tested. The median breast milk perchlorate concentration was 9.1 µg/L. This was about 3 times higher than the median perchlorate concentrations in the urine samples of these women. There was no correlation between breast milk iodine and perchlorate concentrations (R^2 = 0.05, p = 0.1), and no correlation in those women with breast milk perchlorate concentrations above 10 µg/L. The median breast milk iodine concentration was fairly low (median = 155 µg/L; range, 2.7 - 1968) and the authors estimated that 47 percent of the breast milk samples did not contain enough iodine to meet the infant iodine intake recommended by the Institute of Medicine.

Dasgupta *et al.* (2008) measured perchlorate, thiocyanate, and iodine in the urine and breast milk of 13 breastfeeding women. The mean breast milk perchlorate concentration was 9.3 µg/L (SD ± 7.5 µg/L). Selectivity factors were determined for each chemical based on the relative excretion of each in breast milk and urine. Total perchlorate excretion was based on urinary and breast milk excretion only and possible excretion via other pathways was ignored. The median fraction of total excretion in the milk for perchlorate, thiocyanate, and iodine were 0.541, 0.053, and 0.177. The selectivity factors for perchlorate over iodide transport, and thiocyanate over iodide transport, were 3.14 and 0.27, respectively. The authors note that these transport selectivities are an order of magnitude lower than those indicated in *in vitro* studies. The authors did not specifically report a correlation coefficient for the relationship between breast milk iodine and perchlorate concentrations but did note that in their plot of these data (their Figure 3) that there were no subjects in the high iodine-high perchlorate quadrant.

More recently, Valentín-Blasini *et al.* (2011) measured perchlorate in urine samples from 92 infants ages 1-377 days and estimated perchlorate intake doses based on these measurements. The median estimated intake was 0.160 µg/kg-day. Of the 205 individual dose estimates (multiple urine samples were collected from each subject), 9 percent exceeded the NAS (2005) reference dose of 0.7 µg/kg-day. Breast-fed infants had a higher estimated perchlorate exposure dose (geometric mean = 0.220 µg/kg-day) than infants consuming cow milk-based formula (geometric mean = 0.103 µg/kg-day, p < 0.0001) or soy-based formula (geometric mean = 0.027 µg/kg-day, p < 0.0001).

Kirk *et al.* (2013) used data on daily water intake, daily urine volume, predicted daily milk volume, and perchlorate concentrations in water, urine, and breast milk samples from 13 lactating women in Texas to estimate average daily exposure to perchlorate from food and water. The amount of perchlorate from water was estimated by multiplying the amount of daily water intake from each water source

used by the subject by the perchlorate concentration in samples of that water source and summing the results across all water sources. The amount of perchlorate from non-water sources (presumably mostly food) was then estimated by subtracting the estimate of exposure from water from the total amount of perchlorate excreted in urine and breast milk. The mean urinary perchlorate concentration was 3.6 µg/L, with a mean estimated daily urinary perchlorate excretion of 5.8 (±5.3) µg. Total excretion of perchlorate in breast milk was not provided, although based on perchlorate milk concentrations and typical milk consumption rates in infants the authors estimated that the average daily transfer of perchlorate to infants through breast milk was 12.87 (±8.99) µg. Using urine and breast milk perchlorate excretion rates, the mean maternal daily dose of perchlorate was estimated to be 0.186 µg/kg-day with an estimated 0.173 µg/kg-day (93 percent) coming from non-water sources. Importantly, mean perchlorate water concentrations in this population were low (0.46 µg/L ±1.11) so these data are likely not relevant to subjects who live in areas with greater perchlorate contamination in drinking water.

Huber *et al.* (2011) used urinary concentrations of perchlorate measured in the 2001-2 NHANES and drinking water perchlorate concentrations from the U.S. EPA Unregulated Contaminant Monitoring Rule (UCMR) database to estimate the possible amount of perchlorate exposure due to food and water in U.S. adults and children ages 6 and older. The UCMR database included perchlorate water concentrations in a "near census" of 3,086 large public water systems (those serving >10,000 people) and 797 representative small public water systems, measured between 2000 and 2005. NHANES is a large, essentially nationally representative survey performed in the U.S. by the Centers for Disease Control and Prevention. Residential location for NHANES subjects was only available to the researchers on a county-level basis. Subjects in NHANES with urinary perchlorate measurements were divided into one of three bins. Bin I (n=320) included subjects residing in counties where at least one water system had at least one UCMR water perchlorate measurement above the detection limit of 4 µg/L. Bin III (n=2,059) included subjects residing in counties where a drinking water system had been sampled for perchlorate but all measurements were below the detection limit. Bin II (n=325) included subjects who had no UCMR measurements for a water system in the county in which they resided. Estimates of 24-hour perchlorate intake were calculated for all subjects using single spot urinary perchlorate concentrations with adjustments for urinary creatinine. Estimates in Bin III subjects were assumed to represent typical daily exposure from food, while the difference in estimates between Bins I and III was assumed to represent typical daily exposure from water. Overall, the mean estimates were 0.081 µg/kg-day in Bin III (food only) subjects and 0.101 µg/kg-day in Bin I subjects (food + water), and the authors estimated that about 19.7 percent of perchlorate exposure in subjects from exposed counties came from water. Estimates of intakes from water in specific age groups ranged from 2.1percent for ages 6-11 to 25.6 percent for ages 12-19. Overall, these data suggest that food is typically the predominant source of perchlorate for most people in the U.S. Potential weaknesses included the fact that not all water systems were

measured (i.e., many smaller public water systems and all private wells were not measured), the potential impact of fasting was not accounted for, data on the amount of water consumption subjects had from any particular water source was not incorporated, and no estimates were available for children under age 6. Also, the detection limit for perchlorate at the time the water sources were measured was 4 µg/L, so there is little information in this study on the impacts of lower exposures (i.e., those above zero but below 4 µg/L). In addition, many counties have multiple water systems with highly variable perchlorate levels. As such, it is likely that many people in a county with a single positive drinking water perchlorate measurement will actually be drinking water from a system with very low or no perchlorate. The inclusion of these lower exposure people in Bin I would lead to underestimates of the true intake of perchlorate from drinking water. Because of these weaknesses, the specific contribution of perchlorate from water in people who have elevated levels of perchlorate in their drinking water cannot be accurately estimated using the data from this study.

2. METABOLISM AND PHARMACOKINETICS

Absorption

Test data from human studies indicated that perchlorate is readily absorbed from the gastrointestinal tract and excreted primarily via the urine. Eichen (1929; as cited in Stanbury and Wyngaarden, 1952) orally administered 1-2 g perchlorate to patients and recovered 70 percent of the dose in the urine in 12 hours and 85-90 percent in 24 hours. In a similar experiment, two human subjects each drank a solution of 794 mg of sodium perchlorate dissolved in 100 mL of water (Durand, 1938). Fifty percent of the administered dose was recovered in the urine by five hours and 95 percent in 48 hours. These human data suggest absorption of perchlorate through the oral route is virtually complete.

Besides the thyroid, the sodium-iodide symporter (NIS) appears to be expressed and active in mammary gland, salivary glands, gastric mucosa, and placenta (Vayre *et al.*, 1999; Tazebay *et al.*, 2000; de la Vieja *et al.*, 2000; Mitchell *et al.*, 2001). These transport systems exhibit functional similarities with their thyroid counterpart and may play a role in the absorption of iodide into the body. Because perchlorate is completely ionized in aqueous systems, its permeability through intact skin is expected to be limited (U.S. EPA, 1998a). Inhalation exposure during showers is considered possible but not likely to be an important route of exposure. This is because the droplets produced in showers are generally too large to be inhaled. Exposure to vapors of the chemical via the inhalation route is expected to be negligible because of the low vapor pressure of perchlorate salts at room temperature. However, inhalation of airborne perchlorate particles could be an important exposure route in occupational settings. Lamm *et al.* (1999) studied a group of workers in a perchlorate production plant and reported that there was a correlation between airborne perchlorate dust concentration and the amount of perchlorate excreted in urine.

Distribution

Anbar *et al.* (1959) injected white rats and rabbits intraperitoneally with radiolabeled potassium perchlorate (approximately 3-14 mg per animal) and measured the specific activity per gram of tissue in various organs from 30 minutes to 12 hours post administration. The ratio of the specific activity of perchlorate in thyroids versus the specific activity in blood reached a limiting value of 4.3 ± 0.3 in both rats and rabbits, at about 6 hours after the injection. These data demonstrate that the thyroid of these species concentrates perchlorate ions. There were also indications that perchlorate is retained in the salivary gland and testes.

Chow *et al.* (1969) measured perchlorate uptake using radiolabeled perchlorate in male Sprague-Dawley rats. Rats were injected with 0.1, 0.2, or 5.0 meq/kg of perchlorate (14, 28, or 690 mg/kg, respectively) two hours prior to sacrifice. At

the low and middle doses, radiolabeled perchlorate concentrations in the thyroid were higher than those in the blood. At the high dose, perchlorate concentrations in the thyroid and blood were about the same. In a similar study, rats were exposed to 0.69, 1.4, 2.8, 6.9, or 14 mg/kg of perchlorate. The apparent accumulation of perchlorate in the thyroid, as reflected by the thyroid/blood ratio (which ranged from 31.1 to 2.5), was found to be inversely related to the perchlorate dose (U.S. EPA, 2002).

Chow and Woodbury (1970) also studied perchlorate accumulation by the thyroid. They administered perchlorate by intraperitoneal injection at 0.69, 14, or 280 mg/kg to groups of male Sprague-Dawley rats. The treated rats were sacrificed at 0.033, 0.067, 0.13, 0.2, 0.5, 1.0, 2.0, and 4.0 hours after dosing. The amount of perchlorate accumulation in the thyroid compared to that in the plasma was highest at the lowest dose. At the higher doses (at or above 14 mg/kg), the level of perchlorate in the thyroid was lower than in the plasma.

It has been shown that perchlorate inhibits iodide transport into the thyroid. Thyroid tissues can also concentrate several related monovalent anions. Measurement of the ability to be concentrated by thyroid tissues, or to inhibit iodide transport, has resulted in the following potency series for monovalent anion-based inhibition of iodide transport in thyroid slices: $TcO_4^- \geq ClO_4^- > ReO_4^- > SCN^- > BF_4^- > I^- > NO_3^- > Br^- > Cl^-$ (Wolff, 1964; as cited in Wolff, 1998). These relative potencies are based on *in vitro* data and high anion concentrations. It is not clear whether they also apply to *in vivo* scenarios, real-life human situations, or lower environmentally relevant exposure levels. Anbar *et al.* (1959) showed that the inhibition of iodide transport by perchlorate is a truly competitive process. They intraperitoneally injected ^{36}Cl-labeled perchlorate and iodide ions in various concentrations to groups of rats and found that either iodide or perchlorate could inhibit the accumulation of the other anion by the thyroid (Table 4).

Recently, the apparent accumulation of perchlorate by the thyroid of rodents has been disputed. Citing *in vitro* electrophysiological data, de la Vieja (2000) suggested perchlorate acts as a blocker of NIS, but it is not translocated via NIS into the cell. De la Vieja (2000) theorized that because ^{36}Cl chlorate (ClO_3^-) is a byproduct of the reaction employed to chemically synthesize ^{36}Cl perchlorate for the uptake study, it is possible that ^{36}Cl chlorate, rather than perchlorate, accounts for the measured radioactivity, given that chlorate is readily translocated via NIS into the cell.

Table 4. The Ratio between Concentrations of Iodide and Perchlorate Ions in the Thyroid (from Anbar *et al.*, 1959)

Iodide dose (mmol)	Perchlorate dose (mmol)	Ratio[a] I^-/ClO_4^-		
		60 min	120 min	360 min
0.14	0.028	4.7	6.9	3.3
0.14	0.14	2.1	2.7	2.2
0.028	0.14	0.53	0.58	0.67

[a]Ratio = concentration of iodide in thyroid / concentration of perchlorate in thyroid.

Goldman and Stanbury (1973) administered ^{36}Cl-labeled potassium perchlorate to male Sprague-Dawley rats by intraperitoneal injection (approximately 40 μg stable perchlorate per injection). The rats were maintained on a low iodine diet for 4-5 weeks prior to perchlorate administration. The level of perchlorate in the thyroid peaked at four hours after administration, then declined to approximately five percent of its peak at 96 hours. The decay followed an exponential function with a half-life of 20 hours. When the levels of radioactivity in the serum and the urine are plotted against time, they also followed an exponential function with a half-life of approximately 20 hours. Goldman and Stanbury (1973) also showed that most of the administered perchlorate was excreted in the urine. The retention of the radiolabel in selected tissues 96 hours after the administration of perchlorate is shown in Table 5.

There are also data indicating that perchlorate can pass through the placenta and affect the fetal thyroid. Thyroid enlargement and reduction of thyroidal iodide uptake have been detected in fetuses of laboratory animals exposed to perchlorate (see the discussion in the Developmental and Reproductive Toxicity section.)

Selivanova and Arefaeva (1986) administered a single oral dose of perchlorate to rats and observed a two-phase biological decay curve. The first biological half-life ranged from 1-2 hours and accounted for a calculated 96 percent of the dose. The second-phase half-life, which accounted for only four percent of the administered dose, ranged from 72 to 80 hours. Yu *et al.* (2000) injected perchlorate intravenously at doses of 0.01, 0.1, 1, and 3 mg/kg to male Sprague-Dawley rats and monitored the serum concentration of perchlorate over time. The estimated early- and terminal-phase half-lives of perchlorate were 2-3 hours and 12-26 hours, respectively.

Table 5. Percent Dose of ^{36}Cl/g Tissue 96 Hours after Intraperitoneal Injection of ^{36}Cl-perchlorate (from Goldman and Stanbury, 1973)

Organ	Percent dose/g tissue[a]
Thyroid	0.142 ± 0.1
Kidney	0.125 ± 0.09
Spleen	0.098 ± 0.03
Liver	0.048 ± 0.04
Brain	Background

[a]Mean ± standard deviation; each value represents five animals.

The differences in biological half-lives of perchlorate in rats in the studies above (Goldman and Stanbury, 1973; Selivanova and Arefaeva, 1986; Yu *et al.*, 2000) are partly due to the three different routes of administration. The difference may also be explained by the fact that the rats in the study reported by Goldman and Stanbury (1973) had been maintained on a low iodine diet for 4-5 weeks before the administration of perchlorate.

Metabolism

There are data to suggest that perchlorate is not metabolized in humans (Anbar *et al.*, 1959). Four patients were orally administered 200 mg of radiolabeled perchlorate (5 μCi), double labeled with ^{36}Cl and ^{18}O. The perchlorate was excreted unchanged in the urine with the two labels (^{36}Cl and ^{18}O) remaining associated in the same molecule. The results also showed that there was no reduction of perchlorate *in vivo*, as there was very little radioactivity associated with Cl^- and ClO^{3-} ions in urine.

Excretion

As described above, 95 percent of a dose of sodium perchlorate administered orally to human subjects was eliminated in the urine by 48 hours after administration (Durand, 1938). Lamm *et al.* (1999) monitored urinary perchlorate levels of two workers during three days with measurable occupational perchlorate exposure and during the subsequent three days without known perchlorate exposure. The perchlorate body burden, as measured using urinary perchlorate concentrations, increased over the three days of work exposure, with decreases between the 12-hour work shifts. The elimination of perchlorate after the last exposure period appeared to follow a first-order kinetics pattern. The average perchlorate elimination half-lives measured for the two workers were 7.9 and 8.2 hours.

Greer *et al.* (2002) administered oral doses of perchlorate in water to human volunteers and estimated half-life values ranging from 6.0 to 9.3 hours, with an

average value of 8.1 hours. These are similar to those reported in Lamm *et al.* (1999).

Selivanova and Arefaeva (1986) administered a single oral dose of perchlorate to rats, rabbits, and calves at 2, 20, 200, and 600 mg/kg in a single oral dose. They reported that in all cases, little or no perchlorate could be detected in the blood after 72 hours. A majority of the administered perchlorate was excreted in the urine; the feces excreted $\leq$ 8.5 percent. Yu *et al.* (2000) injected perchlorate intravenously to rats at doses of 0.01, 0.1, 1, or 3 mg/kg and reported that between 72 percent and 97 percent of the administered dose was excreted in the urine over a 24-hour period.

3. ADVERSE EFFECTS OF THYROID HORMONE AND IODINE DEFICIENCY

The most important and early effect of perchlorate exposure is its effect on reducing iodide uptake by the thyroid. Significant reduction in iodide uptake can lead to decreased thyroid hormone production. For this reason, this chapter reviews studies of the adverse health effects of iodine deficiency and decreased levels of thyroid hormone. This discussion is preceeded by a brief review of normal thyroid physiology.

Thyroid Physiology

The principal hormones secreted by the thyroid are thyroxine (T4) and triiodothyronine (T3). Iodide is a key component of both. While T4 is produced only by the thyroid gland, about 80 percent of T3 is formed outside the thyroid by deiodination of T4. T4 and T3 influence the growth and maturation of tissues, cell respiration and total energy expenditure, and the turnover of essentially all substrates (including carbohydrates, cholesterol, and proteins), vitamins, and hormones (including the thyroid hormones themselves).

The major components of thyroid hormone are iodide and tyrosine. Tyrosine is generally not the rate-limiting component. Iodine is a trace element, and its uptake into the thyroid can be rate-limiting in thyroid hormone production. Ingestion is the main route of iodine intake. Once ingested, iodine is reduced to iodide (I^-) in the gastrointestinal tract and is readily absorbed into the bloodstream.

Thyroid tissue has a special ability to selectively concentrate iodide from the blood where the concentration is usually very low. The thyroid can actively transport iodide into the thyroid such that the iodide concentration in the thyroid can be several hundred-fold higher than concentrations outside the thyroid. Such concentrations are presumably required to promote efficient thyroid hormone production and patients lacking the ability to concentrate iodide have goiters and are hypothyroid (Wolff, 1998). The molecule that is responsible for transport of iodide into the thyroid is called the sodium-iodide symporter (NIS). The structure and regulation of NIS have been characterized (de la Vieja *et al.*, 2000). Recently mouse NIS has been cloned and transferred into normally non-iodide-transporting cells, and these cells show perchlorate-sensitive iodide uptake capability (Perron *et al.*, 2001). These researchers also found evidence to indicate that the NIS is present in tissues other than the thyroid, including the stomach, lactating mammary gland, small intestine, skin, and brain.

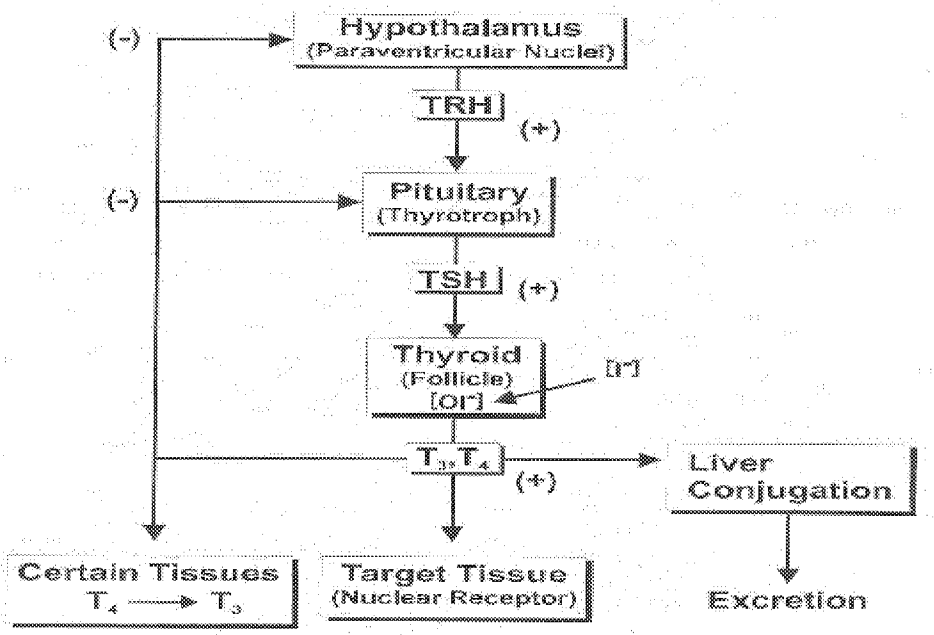
In humans, a majority of T4 and T3 in plasma is bound to proteins. In normal plasma, the T4 protein binding distribution is: 80 percent to thyroxine-binding globulin, 15 percent to transthyretin, and 5 percent to albumin and lipoproteins. For T3, the distribution is 90 percent bound to thyroxine-binding globulin and the

rest to albumin and lipoproteins, with little binding to transthyretin. Very small proportions of T4 and T3 are free (not protein bound) in plasma, 0.03 and 0.3 percent, respectively. Only the free hormone enters cells, exerts its biologic action, and determines thyroid physiologic status (Dillmann, 2000).

Control of T4 and T3 concentrations in blood is mainly regulated by a negative feedback loop involving three organs: the thyroid gland, which produces thyroid hormones; and the pituitary gland and hypothalamus, which respond to and help maintain optimal levels of thyroid hormones (Figure 1). When levels of thyroid hormone decline, the hypothalamus secretes thyrotropin-releasing hormone (TRH), which stimulates the pituitary to produce thyroid-stimulating hormone (TSH), which then prompts the thyroid gland to produce T4 and T3. The stimulated thyroid actively transports iodide into the thyroid gland, and then incorporates the iodide into thyroid hormone molecules. T4 and T3 are metabolized in the liver and other tissues. Some thyroid hormone derivatives are excreted in the bile, and some of the iodide in them is reabsorbed. Cells in the hypothalamus and pituitary gland respond to circulating levels of thyroid hormones, i.e., when hormone levels are high, there is a signal to reduce the output of TRH and TSH. Similarly, when thyroid hormone levels are low, the pituitary is prompted to release more TSH, which stimulates the thyroid to increase thyroid hormone output. This negative feedback loop helps the body to respond to varying demands for thyroid hormone and to maintain hormone homeostasis. Circulating T4, T3, and TSH can readily be measured in the serum of experimental animals and humans and serve as biomarkers of exposure and effect of agents that disrupt thyroid-pituitary status (U.S. EPA, 1998a, and 1998b; Hill *et al.*, 1989).

In mammals, when demands for more thyroid hormone are small, existing thyroid follicular cells can meet the demand. With increased need, as a result of certain chemical exposures or chronic iodine deficiency, the thyroid responds by increasing the size (hypertrophy) and number (hyperplasia) of thyroid follicular cells to enhance hormone output. With continued TSH stimulation, there is actual enlargement of the thyroid gland (goiter) and, at least in rodents, neoplasia of the thyroid follicular cells could eventually occur. Since TSH-producing pituitary cells are also stimulated, they too sometimes undergo hyperplasia and neoplasia (U.S. EPA, 1998b).

Figure 1. Hypothalamic-Pituitary-Thyroid Axis (from U.S. EPA, 1998b)

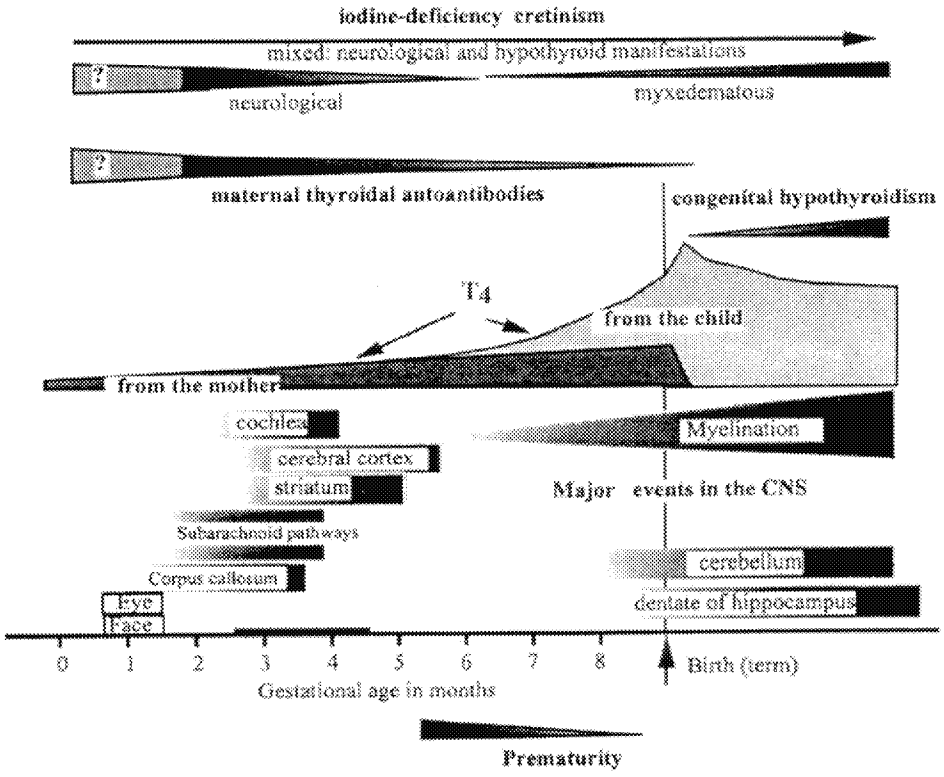


Too much or too little thyroid hormone can lead to illness. Thyrotoxicosis occurs when tissues are exposed to excess amounts of thyroid hormones, resulting in specific metabolic changes and pathophysiologic alterations in organ function. The most frequent cause of thyrotoxicosis is Graves' disease, accounting for 60 to 90 percent of cases (Dillmann, 2000). Graves' disease is an autoimmune disorder with B-lymphocytes producing immunoglobulins, some of which bind to and activate the TSH receptor, stimulating excess thyroid growth and hormone secretion. Hypothyroidism results from decreased secretion of thyroid hormone from the thyroid gland; it can be caused by destruction of thyroid tissues or defects of thyroid hormone production (e.g., congenital enzyme defects, congenital mutations in TSH receptor, iodine deficiency or excess). In some rare occasions, hypothyroidism can also be caused by pituitary or hypothalamic diseases.

The most severe neurological impairment resulting from decreased thyroid hormone production or iodine deficiency is cretinism. Characteristics of cretinism include mental retardation, spastic dysplasia, and problems with gross and fine motor control. In some extreme forms, the affected individuals cannot walk or stand. A number of studies indicate that even less severe iodine deficiency can reduce maternal serum thyroid hormone levels and may subsequently impair the brain development of the offspring (Glorieux *et al.*, 1988; Rovet *et al.*, 1987; Tillotson *et al.*, 1994; Vermiglio *et al.*, 1990; Pop *et al.*, 1999, 2003; Haddow *et al.*, 1999; Bleichrodt and Born, 1994). These studies are reviewed in further detail in the following sections. The nature and severity of the adverse effects are related to the degree of iodine deficiency or the extent of maternal thyroid hormone decrease.

Most data suggest that fetal damage during development is inversely related to maternal serum T4 levels (Pop *et al.*, 2003; Kooistra *et al.*, 2006). Maternal serum free T4 (fT4) is able to pass through the placenta and is converted to T3 in the fetal brain. The T3 generated in the fetal brain is believed to be necessary for the development of the brain, specifically the cerebral cortex, the extrapyramidal system, and the cochlea (Porterfield, 2000). The availability of a minimum level of maternal fT4 is crucial for proper fetal brain development in the first and second trimesters, as the fetal thyroid is not fully mature and functional during that time period. Figure 2 shows the approximate timing of major insults to the brain resulting from hypothyroxinemia (a low level of serum T4), superimposed on major neurodevelopmental events (Morreale de Escobar *et al.*, 2000).

Figure 2. Approximate Timing of Major Insults to the Brain Resulting from Hypothyroxinemia, Superimposed on Major Neurodevelopmental Events.



Thyroid Problems in Pregnant Women with Low Iodine Intake

A number of human studies have shown that pregnancy stresses the thyroid (Crooks *et al.*, 1967; Glinoer *et al.*, 1990, 1992, 1995; Smyth *et al.*, 1997; Caron *et al.*, 1997; Brent, 1999; Kung *et al.*, 2000). In areas of iodine deficiency (e.g., intake level <100 µg/day), there is an increased risk of abnormally low serum T3 and T4 levels, and thyroid enlargement and goiter in pregnant women. The nature and severity of changes in thyroid function are related to the severity of

the iodine deficiency. In an epidemiologic survey reported by Delange and Ermans (1991; as cited in Delange, 1994), the investigators found the prevalence of goiter in an area with severe iodine deficiency is influenced by age and sex, with maximal frequency in females during puberty and childbearing age (Figure 3).

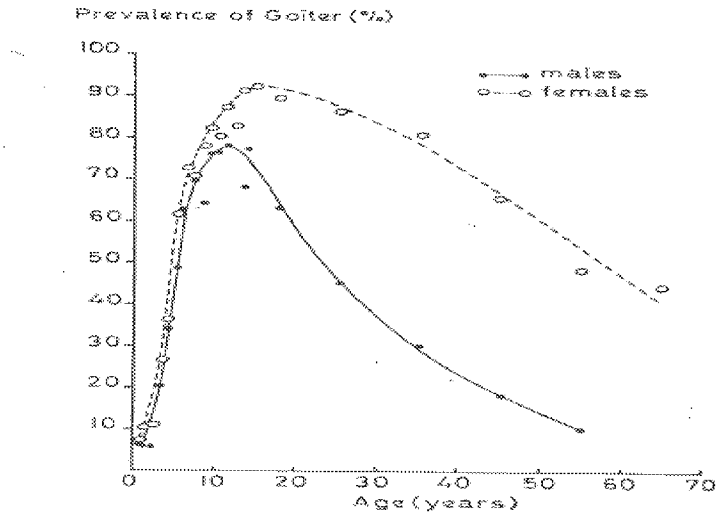


Figure 3. Changes in the Prevalence of Goiter as a Function of Age and Sex in Severe Endemic Goiter (Idjwi Island, Zaire) (Delange, 1994)

Crooks *et al.*, 1967. Crooks *et al.* (1967) studied enlargement of the thyroid gland in pregnant and non-pregnant women in Aberdeen, Scotland and Reykjavik, Iceland. In the Scotland study, they found that the thyroid gland was visible and palpable in 70 percent of pregnant women but in only 37 percent of non-pregnant women in the reproductive age group. By contrast, in the Iceland study, the frequency of thyroid enlargement was about the same in pregnant (23 percent) and non-pregnant women (19 percent). The authors (1967) suggested that the results can be explained by the fact that Icelandic diet is based on fish and contains high levels of iodine. This hypothesis is supported by the significantly higher mean plasma inorganic iodine concentration measured in non-pregnant Icelandic women (0.691 µg/dL) compared to the mean of 0.420 µg/dL found in Scottish non-pregnant women ($p<0.001$).

Glinoer *et al.*, 1990. Glinoer *et al.* (1990) suggested that in conditions of marginally low iodine intake, pregnancy constituted a goitrogenic stimulus. They followed a group of 606 healthy pregnant women in Brussels, Belgium, an area of marginally low iodine intake (50-70 µg/day), and monitored their T3, T4, TSH, and human chorionic gonadotropin (hCG) levels in serum during the first, second, and third trimesters. All subjects were evaluated clinically and determined to be without detectable thyroid abnormality at the beginning of the study. The authors found that a normal thyroid is faced with a triple challenge during pregnancy. First, there is a significant increase in circulating levels of the major T4 transport protein, thyroglobulin (Tg), in response to high estrogen

levels. As a result, the thyroid has to increase its T4 output in order to maintain a stable T4/thyroglobulin ratio of 37-40 percent.

Second, several thyroidal stimulating factors of placental origin (mainly hCG) are produced in excess. This contributes to a decrease of serum TSH (mainly in the first half of gestation) and an increase in thyroid volume (Table 6). They found that during pregnancy thyroid volume increased by an average of 18 percent. This increase was statistically significant and thyroid size increased in a majority of women (73 percent). Goiter, defined as thyroid volume greater than 23 mL, was found in nine percent of the cohort at delivery.

Table 6. Changes in Mean Thyroid Volume in Healthy Women during Pregnancy (from Glinoer *et al.*, 1990)

Stage of Pregnancy	N	Total volume (mL)
First trimester	168	12.1 ± 4.5
Second trimester	172	12.8 ± 4.5
Third trimester	33	13.9 ± 4.8[a]
Delivery	179	15.0 ± 6.8[b]

[a] $p < 0.03$ vs. beginning of pregnancy.
[b] $p < 0.001$ vs. beginning of pregnancy.

Third, pregnancy is accompanied by a decrease in the availability of iodide for the maternal thyroid, due to increased renal clearance (Aboul-Khair *et al.*, 1964; as cited in Glinoer *et al.*, 1990) and losses to the feto-placental complex during late gestation, resulting in a relative iodide deficiency state.

Glinoer *et al.*, 1992. In a related study, Glinoer *et al.* (1992) monitored the thyroid condition of pregnant women in an area without overt iodine deficiency, but with a marginal iodine supply (less than 100 µg/day in 80 percent of women). They found that maternal thyroid function at delivery was characterized by a relative hypothyroxinemia; increased T3/T4 ratios, indicating preferential T3 secretion; slightly increased TSH levels within the normal range in 97 percent of women; increased serum thyroglobulin values, which were above normal in 60 percent of women; and goiter formation in almost 10 percent of women. In the newborns, they found fT4 levels were significantly higher than in the respective mothers. However, mean neonatal TSH and Tg levels were significantly higher than maternal values. Furthermore, these values were highly correlated with maternal data, suggesting the limited availability of iodine was the common link.

In a review paper, Glinoer (2001) again stressed the profound alterations in the thyroid economy associated with pregnancy. In healthy iodine-sufficient pregnant women, this leads to a physiological adaptation of the thyroid and an increased production of thyroid hormones. When gestation takes place in conditions with iodine restriction or deficiency, pregnancy may lead to pathological alterations affecting both thyroid function and the anatomical

integrity of the thyroid gland. The more severe the iodine deficiency, the more obvious, frequent, and profound the potential maternal and fetal repercussions.

Smyth *et al.*, 1997. Supportive results were reported in two other studies, one in Ireland and the other in France. Smyth *et al.* (1997) evaluated ultrasound-measured thyroid volume of 115 pregnant women during one of the three trimesters. These women (Group A) were enrolled based on availability, and each trimester's study group comprised different individuals. Control values for thyroid volume were obtained from 95 pre-menopausal females. All subjects were from Dublin, Ireland, an area of moderately low dietary iodine intake (median urinary iodine was 82 µg/day). All pregnant women studied delivered live-born, normally formed, singleton infants and received no iodine-containing supplements during their pregnancy. The authors reported that the mean thyroid volume of 13.9 ± 0.8 mL, observed in the first trimester, was significantly greater than the control value (11.3 ± 0.5 mL; $p < 0.05$) and reached a maximum of 16.0 ± 0.7 mL, a 47 percent increase ($p<0.01$), in the third trimester.

In a related study, Smyth *et al.* (1997) studied a group of 38 pregnant women (Group B), prospectively. Casual urine samples were collected sequentially during the 3 trimesters of pregnancy and at approximately 6 weeks postpartum. Of those 38 subjects, 20 had thyroid ultrasound scans during each trimester of pregnancy and at 6 weeks postpartum. Thyroid volumes greater than 18.0 mL were defined as enlarged. The number of enlarged thyroids increased from the non-pregnant control value of 6.3 percent, through 19.5 percent in the first trimester, to reach a plateau of approximately 32 percent in the second and the third trimesters, which was maintained up to 40 days postpartum.

Urinary iodine of the women in Group A and Group B were also measured. Urinary iodine measurements collected from 1,063 pre-menopausal women over a one-year period were used for comparison. The researchers found that urinary iodine levels measured throughout the pregnancies of the women in Group A and Group B (Table 7) were higher than in the controls (median 70 µg/L). They suggested that in an area of moderately low dietary iodine intake, urinary iodine loss during pregnancy may result in maternal thyroid enlargement.

Table 7. Median Urinary Iodine Excretion (µg/L) in Pregnancy (Smyth *et al.*, 1997)[a]

	First Trimester	Second Trimester	Third trimester
Group A	135	122	122
Group B	155	122	115

[a]Some of the values were estimated from a graph.

Caron *et al.*, 1997. In a prospective study, Caron *et al.* (1997) evaluated the thyroid condition of 347 pregnant women living in the southwest of France (with an estimated urinary iodine excretion value of 50 µg/day). Iodine concentration in urine samples and serum thyroid hormone measurements were taken at initial

presentation (before 12 weeks of gestation), and during the nine months of pregnancy. Mean urinary iodine levels were low during the first trimester (6.9 ± 0.4 µg/dL), as well as during the ninth month of pregnancy (8.6 ± 0.6 µg/dL). A thyroid ultrasound was performed one to five days after delivery in 246 mothers. During pregnancy fT4 and T3 concentrations decreased ($p<0.001$), and TSH and Tg concentrations increased ($p<0.001$). Thyroid hypertrophy (thyroid volume greater than 18 mL) was present in 29 percent of the mothers. The percentage of thyroid hypertrophy at delivery was associated with urinary iodine concentration during the first trimester of gestation: 15.4 percent (urinary iodine < 5 µg/dL), 9.2 percent (urinary iodine 5-10 µg/dL), and 3.5 percent (urinary iodine > 10 µg/dL) (Figure 4). Goiter (thyroid volume greater than 22 mL) was present in 11 percent of the mothers. The researchers concluded that in areas with a marginally low iodine supply, pregnancy constitutes a goitrogenic stimulus.

Kung *et al.*, 2000. In another prospective study, Kung *et al.* (2000) studied 230 pregnant women living in a borderline iodine sufficient area (Hong Kong). The median urine iodine concentration in healthy adults was 0.77 µmol/L (9.8 µg/dL) in Hong Kong, which was close to the World Health Organization cut-off value of 0.79 µmol/L (or 10 µg/dL) for iodine sufficiency. When recruited into the study, all pregnant women were in their first trimester; subjects with a history of thyroid dysfunction were excluded. These women were prospectively studied at approximately 12-14 weeks, 20-24 weeks, and 36 weeks of gestation, as well as 6 weeks and 3 months postpartum for thyroid function, thyroid volume by ultrasound examination, and urine iodine concentration. Study results are presented in Table 8. The investigators showed that in an area of borderline low dietary iodine intake, pregnancy was an important stress to the maternal thyroid axis. Pregnancy caused an average 30 percent increase (range, 3 – 230 percent) in thyroid volume, with some subjects having a more than two-fold increase. This thyroid enlargement persisted and failed to revert completely even 3 months after delivery.

The researchers also reported that 14 women with excessive thyroidal stimulation in the second trimester had lower urine iodine concentrations and larger thyroid volumes throughout pregnancy. Furthermore, their neonates had higher cord TSH, Tg, and slightly higher thyroid volumes than the neonates of 216 pregnant women without evidence of thyroid stimulation. Seven neonates (50 percent) born to these women had subnormal fT4 levels at birth.

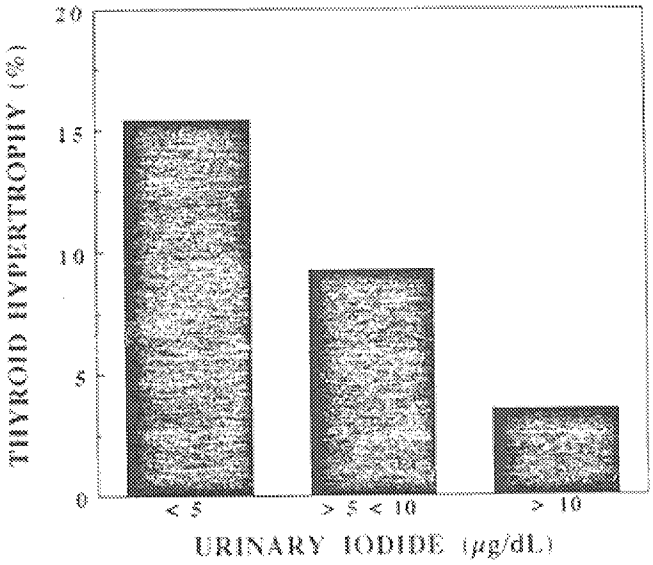


Figure 4. Percentage of Maternal Thyroid Hypertrophy in Relation to Urinary Iodine Concentration during the First Trimester of Pregnancy (Caron *et al.*, 1997)

Table 8. Change of Thyroid Function Tests, Thyroidal Volume, and Urinary Iodine Level of Women during and after Pregnancy (Kung *et al.*, 2000)

	First trimester	Second trimester	Third trimester	Postpartum 6 weeks	Postpartum 3 months
Total T4 (nmol/L)	154 (132-176)	126 (110-143)[a]	125 (106-142)[a]	89 (81-98)[b]	92 (82-101)[b]
Free T3 (pmol/L)	3.9 (3.6-4.3)	3.4 (3.1-3.7)[a]	3.3 (3.0-3.7)[a]	4.0 (3.7-4.4)	4.3 (4.1-4.6)
Free T4 (pmol/L)	13.4 (12.2-15.0)	11.9 (10.7-13.1)[a]	11.7 (10.1-13.0)[a]	14.5 (13.1-16.0)	14.4 (13.0-15.8)
TSH (mIU/L)	0.49 (0.12-1.00)	0.96 (0.62-1.28)[a]	0.95 (0.60-1.36)[b]	1.15 (0.74-1.58)[b]	1.14 (0.81-1.61)[b]
Urine iodine (μmol/L)	0.84 (0.60-1.09)	0.91 (0.65-1.14)[a]	0.98 (0.72-1.24)[a]	0.83 (0.56-1.08)	0.79 (0.51-1.14)
Thyroid volume (mL)	9.5 (7.2-12.3)	10.3 (7.7-13.6)[a]	11.2 (8.9-13.8)[a]	11.0 (8.3-14.2)[a]	10.6 (8.6-13.7)[a]

Results are medians
[a] $p < 0.05$ vs. first trimester
[b] $p < 0.01$ vs. first trimester

Another source of data supporting the concept that normal pregnancy requires increased thyroid hormone production comes from the observation that women previously diagnosed with hypothyroidism on adequate T4 replacement doses often require an increase in their T4 doses during pregnancy (Table 9).

Table 9. Thyroid Hormone Requirement in Pregnancy (Brent, 1999)

Study	Mean daily dose (µg)	Fraction of women requiring an increased dose	Mean dose increase for those who had an adjustment (µg)
Pekonen *et al.* (1984)	141	7/34 (21%)	62
Mandel *et al.* (1990)	148	9/12 (75%)	46
Tamaki *et al.* (1990)	-	4/4 (100%)	-
Girling and de Swiet (1992)	142	9/32 (28%)	68
Kaplan (1992)	154	27/42 (64%)	42
Pooled data	146	56/124 (45%)	46

Romano *et al.*, 1991; Pedersen *et al.*, 1993; Glinoer *et al.*, 1995. These are three prospective studies showing that in an area with marginal or moderate iodine deficiency, iodine supplementation often can reduce the stress on the thyroid during pregnancy. The first study was carried out in L'Aquila, Italy, an area with moderate iodine deficiency (Romano *et al.*, 1991). There were 35 pregnant women in the study, all of whom had a normal pregnancy and no history of thyroid disease. They had a mean age of 27.1 years (±3.8) and a mean body weight of 61.6 kg (± 4.9) at the first examination during the first trimester. Pregnant women were randomly assigned into group A (n=17) or group B (n=18). Immediately after the first examination, iodide salt equivalent to a daily intake of about 120 to 180 µg iodide was prescribed to all the women in group A. Each trimester all pregnant women in both groups were subjected to three ultrasonographic evaluations of thyroid volume and to measurement of body weight. During each examination, 24-hour urine samples were also taken to determine the iodine urinary excretion. Romano *et al.* (1991) reported that TSH levels of all the subjects were within the normal range and TSH levels measured in group A did not statistically differ from those measured in group B. The effect of iodine supplementation was confirmed by urinary iodine measurements. A significant increase in urinary iodine excretion was found at the second and third examination ($p<0.0001$ and $p<0.01$, respectively, Table 10) only in group A, treated with iodide salt.

Table 10. Iodine Excretion (µg/24 hours) in Both Groups at Each Trimester (mean± standard deviation) (from Romano *et al.*, 1991)

	First trimester	Second trimester	Third trimester
Group A	37.0±36.0	154.0±59.0[a]	100.0±39.0[b]
Group B	30.5±42.0	55.0±35.0	50.0±37.0

[a]$p<0.0001$
[b]$p<0.01$ vs. first trimester

Thyroid volume did not change throughout pregnancy in the group treated with iodide salt. However, in the control group (Group B) there was a statistically significant increase in thyroid volume from the first to the third trimester (mean increase = 1.6 ± 0.6 mL; $p<0.0001$). Romano *et al.* (1991) concluded that an adequate dietary iodine intake is necessary to prevent the development of gestational goiter, and iodine deficiency is the main causative factor of thyroid enlargement during pregnancy.

A similar study was also carried out in East Jutland, Denmark, an area with a median daily urinary iodine excretion around 50 µg (Pedersen *et al.*, 1993). The researchers selected 54 normal pregnant women and randomly divided them into iodine-treated (28 subjects) and untreated groups (26 subjects). Before iodine supplementation was initiated, the measured variables were nearly identical in the two groups. Treated subjects received 200 µg iodine/day starting from weeks 17-18 of pregnancy until 12 months after delivery. All women were followed at regular intervals during pregnancy. In the control group, serum TSH, serum Tg, and thyroid size showed significant increases during pregnancy. These variations were less in the iodine supplementation group (Figures 5, 6, and 7).

Iodine did not induce significant variations in serum T4, T3 or free T4 in this study. Pedersen *et al.* (1993) concluded that a relatively low iodine intake during pregnancy leads to thyroid stress, with increases in Tg release and thyroid size. It is important to note that even in the iodine-supplement group, there was a significant increase in thyroid volume during pregnancy. Notably, the size of the thyroid returned to initial values one year after delivery independent of iodine supplementation. Pedersen *et al.* (1993) were concerned that thyroidal stress during pregnancy in an area of iodine deficiency can lead to goiter, which is primarily reversible, as was shown in the study. However, at some point iodine deficiency triggers, by an unknown mechanism, irreversible changes in the thyroid with autonomous growth and function and may lead to high incidence of multinodular toxic goiter in elderly subjects. It was suggested that iodine deficiency during pregnancy or even during fetal life could be an important factor for the late development of thyroid autonomy.

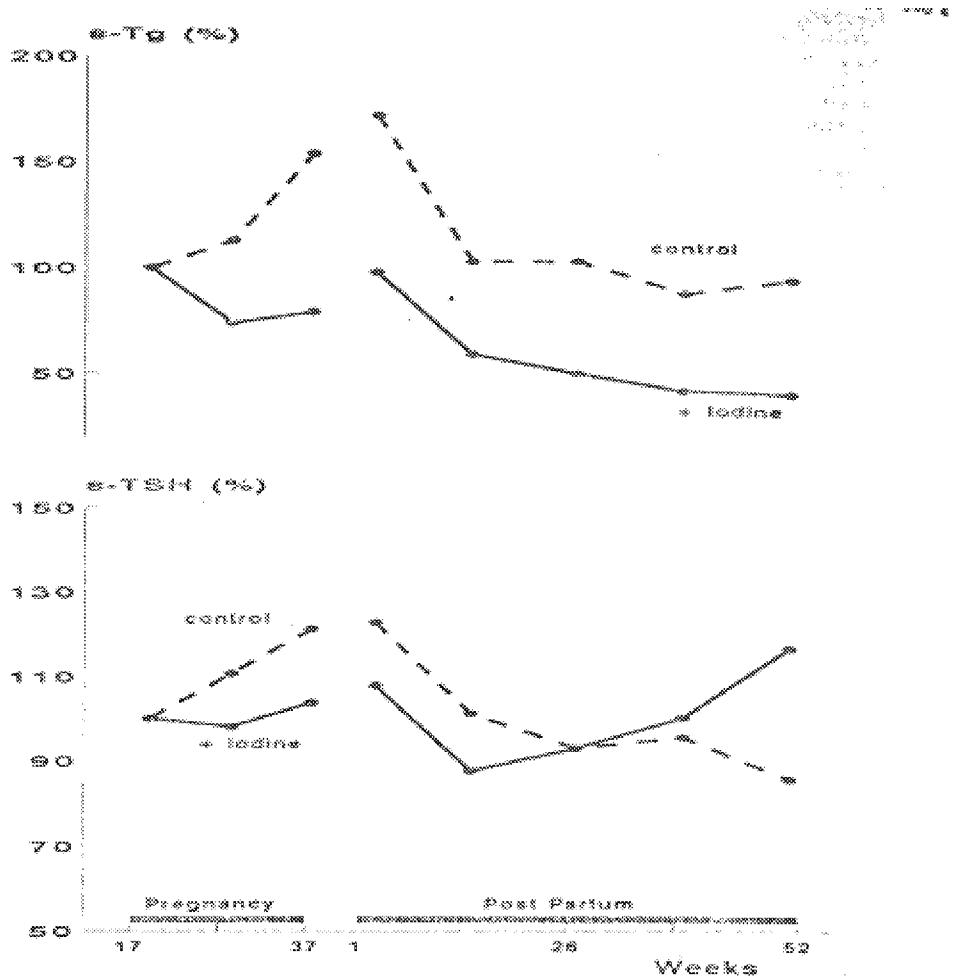


Figure 5. Serum Tg and TSH during Pregnancy and for 52 Weeks Postpartum in Women Receiving Iodine Supplementation and Control Women, as a Percentage of the Initial Values (from Pedersen *et al.*, 1993). Median values are shown. The increase in serum Tg during pregnancy in the control group was statistically significant ($p<0.01$), but the first value obtained during pregnancy and the values obtained one year after delivery were not different. Tg values from the two groups were significantly different at all periods, except before initiation of iodine supplementation. The increase in serum TSH in the control group during pregnancy was statistically significant ($p<0.01$), whereas no differences between values were found in the iodine supplemented group ($p=0.29$, by Friedman's test). During the postpartum period, no significant TSH differences between the groups were found.

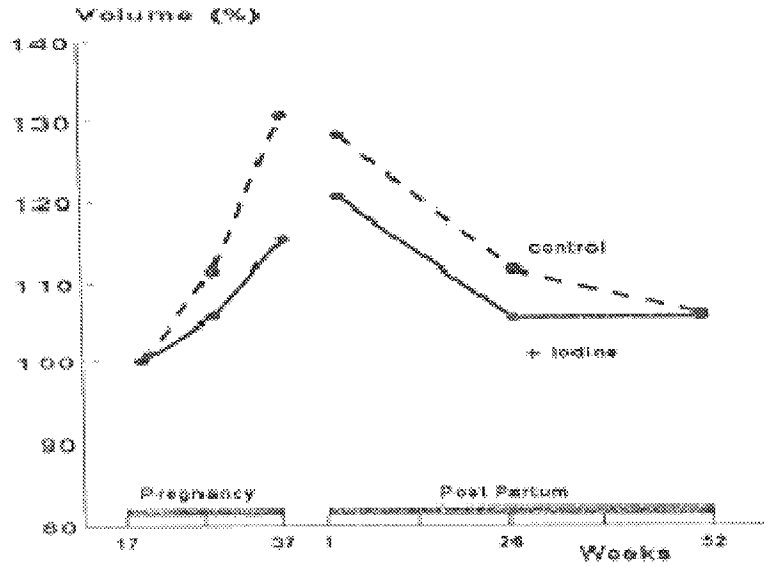


Figure 6. Median Thyroid Volume during Pregnancy and 52 Weeks Postpartum in Women Receiving Iodine Supplementation and Control Women, as Percent of Initial Values (from Pedersen *et al.*, 1993). In both groups, statistically significant increases during pregnancy and decreases during the postpartum period were found ($p<0.05$). The increase during pregnancy in controls was higher than that in the iodine supplemented group ($p<0.05$).

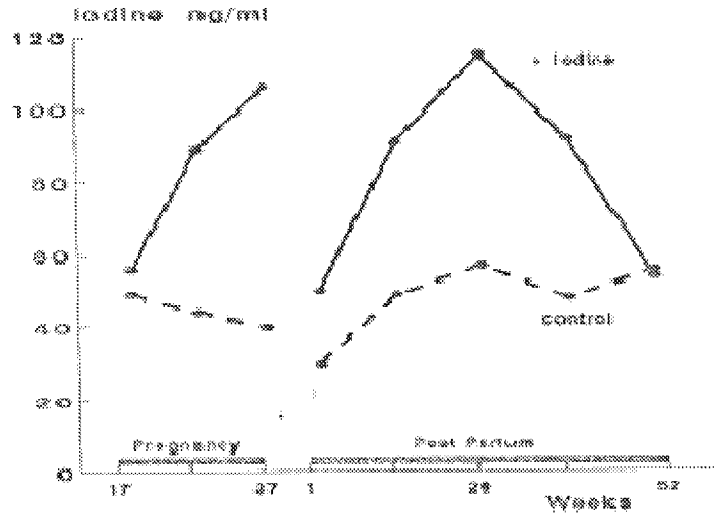


Figure 7. Iodine Concentration in Spot Urine Samples during Pregnancy and for 52 Weeks Postpartum in Women Receiving Iodine Supplementation and Control Women (Pedersen *et al.*, 1993). The last sample was obtained after iodine supplementation was stopped.

Glinoer *et al.* (1995) studied a group of euthyroid pregnant women with mild to moderate iodine deficiency and found pregnancy-related stresses on the thyroid could be prevented by the administration of potassium iodine or potassium iodine plus thyroxine (L-T4). They selected 180 pregnant women at the end of the first trimester on the basis of biochemical criteria of excessive thyroid stimulation, defined as serum thyroglobin > 20 µg/L associated with a low normal fT4 index (<1.23) and/or an increased T3/T4 ratio (>$25x10^{-3}$). The subjects were randomized in a double-blind protocol into three groups and treated until term with either placebo (Group A), potassium iodine (100 µg/day) (Group B), or potassium iodine (100 µg/day) plus L-T4 (100 µg/day) (Group C). At the beginning of the study, all the subjects were mildly or moderately iodine deficient as indicated by a median urinary iodine concentration of 36 µg/L. Only 10 percent of women had urinary iodine above 80 µg/L. After therapy was instituted, the urinary iodine concentrations in Groups B and C rose to approximately 75-130 µg/L in the second and third trimesters; while urinary iodine of Group A remained low during gestation and at delivery.

Study results showed that total T4 levels of all groups increased during the second and third trimesters compared to those measured during the first trimester. However, the increases observed in Group A (4 percent and 7 percent for the second and third trimesters, respectively) were much smaller than those observed in Group B (9 percent and 11 percent) and Group C (19 percent and 15 percent). Glinoer *et al.* (1995) also reported that in Groups A and B, the ratios of T3/T4 were higher than normal at the start of the therapy and remained elevated during gestation. However, in Group C the ratios decreased rapidly toward normal and were maintained at a level of approximately 22 x 10^{-3}. These results indicated that thyroid stimulation associated with pregnancy and leading to preferential T3 secretion by the thyroid was suppressed after potassium iodide plus L-T4 administration. Glinoer *et al.* (1995) found an average increase of 30 percent in thyroid volume in Group A. Sixteen percent of the women in this group developed a goiter during gestation, with thyroid volumes up to 34 mL at delivery. The increment in thyroid volume was much less in Group B (mean increase of 15 percent) and in Group C (mean increase of 8 percent). Furthermore, goiter formation in Groups B (10 percent) and C (3 percent) was less frequent than that in Group A. In the same study, Glinoer *et al.* (1995) also evaluated the thyroid status of the newborns, 3-6 days after delivery. They found that the mean thyroid volume of newborns in Group A (1.05 ± 0.05 mL) was significantly larger than those in Groups B (0.76 ± 0.05 mL) and Group C (0.75 ± 0.05 mL). Furthermore, glandular hyperplasia (thyroid volume >1.4 mL) was found in 10 percent of newborns in Group A (range 1.5-2.2 mL) compared to none in Groups B and C ($p=0.01$, by χ^2 test). Glinoer *et al.* (1995) found the study results in agreement with other investigations on goitrogenesis during pregnancy in areas with less than adequate iodine supply.

Rotondi *et al.*, 2000. This study found an association between thyroid size and the number of their previous pregnancies in an area with moderate iodine deficiency. The researchers studied the size of thyroids of 208 non-goitrous

healthy females by ultrasound examination. All subjects lived in a region (Naples, Italy) that is known to have moderate iodine deficiency, with usual urinary levels ranging from 40-100 µg/day. All subjects had serum free T3, fT4, and TSH measurements, as well as thyroglobulin antibody and thyroid peroxidase antibody detection. All subjects were clinically and biochemically euthyroid and had no detectable thyroid autoantibodies. The subjects were divided into five groups, according to the number of completed pregnancies (0, 1, 2, 3, 4 or more term pregnancies). The researchers found mean thyroid volume increased progressively among the groups; group 0 (14.8±0.7 mL); group I (16.0±0.9 mL); group II (17.1±0.6 mL); group III (18.2±0.6 mL); group IV (20.3±0.9 mL). The difference in the increases in thyroid volume was statistically significant between group 0 and groups III ($p<0.01$) and IV ($p<0.001$), and also between group I and group IV ($p<0.05$). No independent effect of body weight and age on thyroid volume was seen. Based on the results, Rotondi *et al.* (2000) suggested that, in an area with moderate iodine deficiency, there is a cumulative goitrogenic effect of successive pregnancies and the goitrogenic effect of pregnancy is not fully reversible.

As shown above, several studies have identified associations between pregnancy and increased thyroid size. However, as we review in the following paragraphs, this effect has not been seen in all studies.

Gerghout *et al.*, 1994. These researchers studied 10 healthy women before and during a normal pregnancy in an iodine replete area of Amsterdam, the Netherlands. They found no change in thyroid volume during pregnancy (data given before pregnancy and during first, second, and third trimesters, respectively: 10.3 ± 5.1, 10.6 ± 4.4, 9.6 ± 3.8, and 9.4 ± 3.0 mL. Urinary iodine levels or dietary iodine intakes were not reported.

Long *et al.*, 1985. These researchers studied a group of pregnant teenagers and found the frequency of goiter in this group was not higher than that in non-pregnant teenagers. They studied 309 consecutive pregnant adolescent girls who were admitted to a medical center in San Diego, California from August 1978 through December 1982. A group of 600 adolescent girls was used as controls to establish the prevalence of goiter in non-pregnant adolescents. The mean gestational age for the first visit was 22 weeks. A thyroid gland was defined as enlarged if it was visible and/or palpable and had a transverse span of $\geq$ 6 cm. Eighteen goiters (6 percent) were identified in the pregnant teenagers versus 27 goiters (5 percent) in the control group. It should be noted that the detection method used in the study is not as sensitive and reliable as the ultrasound detection used in the more recent studies. Long *et al.* (1985) concluded that abnormalities of size and function of the thyroid gland were not more prevalent during the stress of reproduction at a young age.

Levy *et al.*, 1980. This study examined the thyroid glands of 49 matched pairs of women in Ohio, one pregnant and one non-pregnant woman per pair. All pregnant women were at least 20 weeks into the pregnancy and had no personal

history of thyroid abnormality. The subjects were paired by race and age (within 5 years) and examined by multiple observers. Observers independently graded each thyroid as "not palpable," "palpable but not enlarged," or "enlarged." They also compared the size of the two glands relative to one another for every pair of subjects. Levy *et al.* (1980) found that in 22 pairs the pregnant woman had the larger thyroid, whereas in 20 pairs the opposite was true. In six pairs the thyroid glands were not palpable, and in one pair the thyroid glands were of equal size. Five pregnant and three nonpregnant women had clinically significant goiters. None of the differences was statistically significant. These results are consistent with the study of Crooks *et al.* (1967) conducted in Reykjavik, Iceland, which showed that pregnancy did not impact the thyroid gland when iodine intake was adequate.

Liberman *et al.*, 1998. This investigation studied the serum T4, TSH, and serum and urinary inorganic iodine levels during the first, second, and third trimesters and after delivery of 16 women. They reported significantly higher levels of mean serum T4 during the pregnancy than after delivery. Similar levels of serum TSH, serum inorganic iodine, and urinary iodine were measured during pregnancy and after delivery. The daily iodine intakes of the subjects were high, as indicated by the relatively high average urinary iodine levels (459 – 786 µg/day). Liberman *et al.* suggested that pregnancy does not have an important influence on serum inorganic iodine or thyroid status in iodine-sufficient regions.

Adverse Neurological Development with In Utero Iodine Deficiency or Low Thyroid Hormone Levels

The changes in thyroid function associated with pregnancy are related to increased hormone requirements. The need can only be met by a proportional increase in hormone production and is dependent upon the availability of iodine in the diet (Glinoer, 2001). The National Academy of Sciences has recommended an Estimated Average Requirement of 160 µg/day and a Recommended Dietary Allowance of 220 µg/day for pregnant women (NAS, 2001). These values are higher than the Estimated Average Requirement of 95 µg/day and the Recommended Dietary Allowance of 150 µg/day for non-pregnant adults (age 19 years and older).

Iodine deficiency disorders range from endemic cretinism to endemic goiter and less severe forms of brain abnormalities. The impact of iodine deficiency differs depending on the age and life stage of the affected individual, as well as the degree of iodine deficiency. The most severe problems caused by iodine deficiency are among fetuses, neonates, and infants because of the irreversible changes that can occur during this period of rapid structural and behavioral development. Cognitive impairment is the most common finding seen with iodine deficiency, and thyroid disorders during pregnancy have been shown to increase the risk of neurologic damage in offspring (Hetzel and Maberly, 1986; as cited in Hollowell and Hannon, 1997). It was considered a paradox that in areas of iodine deficiency, children with cretinism, but with functioning thyroid glands, had

more severe central nervous system damage than some children who were missing a thyroid gland. For prevention of central nervous system damage, iodide has to be supplied before conception or early in the first trimester, a time in development before the fetal thyroid is known to be functional (Hollowell and Hannon, 1997). The finding that maternal T4 reaches the fetus (Vulsma *et al.*, 1989) made it understandable that maternal thyroid hormones are necessary for brain development during early fetal development, and severe central nervous system damage can occur as a result of maternal thyroid deficiency.

This theory is supported by the results of a number of animal and human studies.

Animal Studies in Neonates Born to Dams with Iodine Deficiency or Low Thyroid Hormone Levels

Obregon *et al.*, 1984 and Woods *et al.* , 1984 and others. Obregon *et al.* (1984) and Woods *et al.* (1984) showed that fetal rat tissues, including brain, contained T4 and T3 before fetal thyroid hormone was produced. Several researchers also reported that nuclear T3 receptors in brain tissues obtained from rat and human fetuses early in gestation (before the development of the fetal thyroid) were relatively saturated with T3 (Bernal and Pekonen, 1984; Perez Castillo *et al.*, 1985; Ferreiro *et al.*, 1988; as cited in Burrow *et al.*, 1994). The presence of occupied T3 nuclear receptors in brain tissues early in fetal development supports a role for maternal thyroid hormones in the maturation of the brain.

Argus Research Laboratories, 1998a and 2001. In two animal developmental studies (discussed in an earlier section), ammonium perchlorate was administered to female Sprague-Dawley rats via drinking water at target doses between 0.01 and 30 mg/kg-day. Morphometric analysis of the pups revealed significant changes in sizes of a number of brain regions (e.g., corpus callosum), although a simple dose-response relationship was not observed for any of the changes (Figure 11).

Potter *et al.*, 1982 and Hetzel *et al.*, 1987. Severe iodine deficiency has been shown to cause abnormal fetal brain development in a number of animal species. Potter *et al.* (1982) reported that severe iodine deficiency in sheep caused reduction in fetal brain weights and in brain DNA and protein from 70 days of gestation to parturition. They also found unusual morphological changes in both the cerebral hemispheres and the cerebellum of the fetal brains. Hetzel *et al.* (1987) reported that severe iodine deficiency caused abnormal fetal brain development in rat, marmoset, and sheep. The abnormalities included reduced brain weight, change in cell density in the cerebral hemispheres, reduced synaptic counts in the visual cortex, and reductions of brain DNA and brain protein.

Lavado-Autric *et al.*, 2003. In this study, the investigators evaluated the effects of a low iodine diet (LID) with (LID-2) or without (LID-1) 1 percent potassium perchlorate in pregnant rats. The potassium perchlorate was used to produce hypothyroxinemia in the pregnant rats. Cell migration and cytoarchitecture in the somatosensory cortex and hippocampus of the 40-day-old offspring were examined (n = 5-7 pups per group). The number of dams per group was not provided. According to the authors, the reproductive performance of the LID-2 animals and the post-natal growth of their pups were normal (although no details are provided). Serum T4 levels were 90 percent lower in both the LID-1 and LID-2 dams than in controls. Levels of serum T3 (the hormonally active form of thyroid hormone) in the LID-1 and control dams were similar. The mean T3 in the LID-2 dams was lower than controls, although the difference was much less than that seen for T4 (mean serum T3 (in ng/mL) in controls: 0.73 ± 0.02 (standard error); in LID-1 animals: 0.65 ± 0.15; in LID-2 animals: 0.37 ± 0.06). Litter size, body weight or postnatal growth measures were not affected.

Using BrdU labeling of cells at specific time points of development, the authors took advantage of the normal migration patterns of cortical neuronal cells to investigate the impacts of thyroid deficiencies on normal structural brain development. Normally, cells born later migrate past cells born earlier and occupy more superficial layers of the cortex. When BrdU was administered on gestation days 14-16, there was a decrease in the proportion of BrdU-labeled cells in the deeper cortical layers and an increase in the subcortical white matter in the LID-1 and -2 offspring compared to controls. The researchers noted that gestation days 14-16 are before the fetal thyroid begins producing thyroid hormone (which usually starts around day 17.5-18). As such, these effects are likely due to deficiencies in maternal thyroid hormones rather than any deficiency of the fetal thyroid. When BrdU was administered on gestation days 17-19, there was a decrease in labeled cells in the superficial layers and an increase in the deeper layers of the cortex. The researchers used single- and double-label immunostaining to find that the BrdU-labeled cells were neurons, not glia.

Overall, these findings provide evidence that the normal pattern of neuronal cell migration in the cortex during fetal development can be disrupted by maternal hypothyroxinemia. In addition, since these effects were assessed in the offspring at postnatal day 40, these findings likely represent permanent rather than temporary alterations to the cortical cytoarchitecture (Zoeller, 2003). This study was different from earlier studies because the level of maternal hypothyroidism introduced was relatively mild and treated pups or dams could not be distinguished from controls by their weight, growth, reproductive performance, or physical appearance. In previous studies, severe hypothyroidism was introduced in the dams of pups by surgical thyroidectomy or strong goitrogens such as high dose methimazole.

The results of this study could potentially provide some mechanistic explanation for the findings in human studies which have linked decreases in maternal thyroid hormone during pregnancy to subsequent altered neurological development in

the offspring (e.g., Pop *et al*., 1999, 2003; Haddow *et al*. 1999). Migration defects in the brain have been associated with neurological deficits in humans (Sun *et al*., 2002). However, it is not currently known how the particular effects seen in this study might impact long-term neurological function.

Auso *et al*., 2004. Normal rat dams were given the goitrogens 2-mercapto-1-methylimidazole on gestation days 12 through 15. Maternal thyroid hormone levels decreased transiently by about 30 percent compared to normal values. There were no clinical signs of hypothyroidism. Mean T4 (± SEM) in the treated and control dams was 11.60 ± 0.67 and 15.90 ± 1.89, respectively. BrdU was injected from gestation days 14-16 or 17-19 and pups were tested for audiogenic seizure susceptibility 39 days after birth. The cytoarchitecture and radial distribution of the BrdU-labeled neurons on postnatal day 40 were affected in 83 percent of the pups from the treated dams. Infusion of T4 at gestation days 13-15, but not during days 15-18 avoided these alterations. An increase in seizures and wild runs in response to acoustic stimulus was seen in the pups from treated dams versus controls. These data provide evidence that transient and relatively mild decreases in maternal T4 during early pregnancy can lead to permanent architectural changes in the brain.

van Wijk *et al*., 2008. This report describes how a lack of thyroid hormone during early development can result in multiple morphological and functional alterations in the developing brain of Wistar (HsdCpb:WU) rats. The behavioral effects of perinatal and chronic hypothyroidism during development in offspring (male and female) of hypothyroid rats were assessed. Twelve dams (starting 2 weeks prior to mating) and offspring (one litter per dam, eight pups per litter) were fed an iodine-poor diet and drinking water with 0.75 percent sodium perchlorate. This continued either until weaning (perinatal hypothyroidism) or until the day of killing (chronic hypothyroidism). The pups were tested for neuromotor competence, locomotor activity and cognitive function until postnatal day 71, comparing them to age-matched control rats. Early neuromotor competence, as assessed in the grip test and balance beam test, was impaired in both chronic and perinatal hypothyroidism groups. The open field test, assessing locomotor activity, revealed hyperactive locomotor behavioral patterns only in the chronic hypothyroid animals. The Morris water maze test assessed cognitive performance and showed that chronic hypothyroidism affected spatial memory in a negative manner, with perinatal hypothyroidism impairing spatial memory in female rats only. Overall, the effects of chronic hypothyroidism appeared to be more pronounced than the effects of perinatal hypothyroidism. This suggests that the early effects of hypothyroidism on functional alterations of the developing brain depend on the timing of the thyroid hormone deficiency during development and the impacts may be decreased, but not eliminated, if the deficiency is improved.

Gilbert and Sui, 2008. These investigators exposed 106 pregnant Long-Evans rats to 0, 30, 300, or 1,000 ppm perchlorate in drinking water (equivalent to 0, 4.5, 44.2, or 140.3 mg/kg-day) from gestation day 6 until weaning (postnatal day

30). Adult male offspring from an unstated number of litters/group were studied with a series of behavioral tasks. These included motor activity as a general test of neurotoxicity (8-11/group), the Morris maze as a spatial learning test (11-17/group), and fear conditioning as a reflection of the integrity of the hippocampus (number of animals unstated). The authors also utilized neurophysiologic measures of synaptic function in the hippocampus including long-term potentiation (LTP), a well-established model of synaptic plasticity (14-17/group). There was no positive control. In the dams, T4 was reduced relative to controls by 16 percent, 28 percent, and 60 percent in the 30, 300, and 1,000 ppm dose groups, respectively. Little change was seen in T3 across dose groups and TSH levels were only increased in the highest dose group (1,000 ppm). Perchlorate dose was not associated with body weight in the dams or pups, or with pup eye opening, brain or hippocampal weights.

In the pups, small decreases (i.e., 10-20 percent) in serum T3 and T4 were seen in the two higher dose groups compared to controls on postnatal day 21. However, all serum hormone levels returned to control levels in adulthood. Perchlorate exposure did not affect motor activity, spatial learning, or fear conditioning in the male offspring at ages 3-13 months. Significant reductions in baseline synaptic transmission were observed in hippocampal field potentials at all dose levels. This included reductions in synaptic transmission at the perchlorate dose that only marginally reduced (about 16 percent) circulating levels of thyroid hormone in dams (30 ppm, 4.5 mg/kg/day).

The Morris water maze failed to uncover spatial learning deficits in perchlorate-treated animals despite the observations of altered hippocampal synaptic transmission coupled with spatial learning impairments after thyroid hormone disruption induced by propylthiouracil (PTU) or methimazole noted in this report and in contemporary studies in perchlorate treated animals. Perhaps these differences are related to sex. This study examined only male offspring, while in the van Wijk *et al.* (2008) study discussed above, spatial memory effects were only seen in females. It may also be related to differences in the mechanism of toxicity or dosimetry compared to PTU and methimazole.

The lack of behavioral effects in the specific tasks used by Gilbert and Sui (2008) may also be a function of dose, degree of hormonal disruption, or the duration of prenatal exposure. Given the cognitive demands and sensitivity of the behavioral tasks, such outcomes are understandable. The failure of perchlorate to detrimentally impact hippocampal LTP is consistent with a lack of effect on behavioral plasticity and it is possible that the augmentation of PS (population spike) LTP is a reflection of an adaptive or compensatory response in cell physiology that aids in the reversal of learning deficits. Also, many other brain regions are engaged in the performance of simple learning tasks, and significant behavioral compensation may mask underlying behavioral deficits apparent earlier in development or revealed with more demanding cognitive tasks. Despite the lack of behavioral effects in the specific tasks used, the changes seen in synaptic transmission in adult offspring nevertheless provide evidence in

a rodent model that modest degrees of thyroid hormone reduction induced by perchlorate result in persistent alterations in brain function.

Human Studies of Infants Born to Mothers with Iodine Deficiency or Low Thyroid Hormone Levels

Many human studies have been published that demonstrate maternal thyroid deficiency during pregnancy affects neuropsychological development of the child. Some of the studies have shown that these effects may occur at thyroid hormone levels that have been traditionally considered to be within normal ranges.

Man and Jones, 1969. Man and Jones first reported that maternal hypothyroidism was associated with lower intelligence quotient scores (IQs) in 8-month-old infants. Hypothyroidism was defined in this study by two low serum butanol-extractable iodine test values during pregnancy or by one low serum butanol-extractable iodine value with clinical hypothyroidism. They found that 81 percent of 26 infants of women given thyroid replacement therapy after two low serum iodine tests were classified "normal," approximately the same percentage as for infants of euthyroid women. In contrast, only 48 percent of the 56 infants of women with two low serum iodine values who were not given adequate thyroid replacement therapy were "normal."

Glorieux *et al.*, 1985. These authors reported that children with significantly retarded skeletal maturation at the time of diagnosis, signifying hypothyroidism *in utero*, obtained lower global IQs than did children whose skeletal maturity was within normal limits.

Glorieux *et al.*, 1988. In a later study, Glorieux *et al.* studied 43 infants with congenital hypothyroidism and found that low T4 (<2 µg/dL) and retarded bone surface (<0.05 cm^2) measurements taken before therapy initiation were strongly correlated with mental development at 3, 5, and 7 years of age (Table 11).

Table 11. Mental Outcome in Infants with Congenital Hypothyroidism Relative to Newborn Risk Criteria (Glorieux *et al.*, 1988)

Age in years	T4 < 2 µg/dL and bone surface measures < 0.05 cm^2			T4 > 2 µg/dL and/or bone surface measures > 0.05 cm^2		
	n	Mean IQ	IQ distribution	n	Mean IQ	IQ distribution
3	17	91 ± 4[a]	(61 – 120)	40	103 ± 2	(81 – 140)
5	14	88 ± 3[b]	(60 – 109)	30	104 ± 2	(84 – 125)
7	16	86 ± 3[b]	(49 – 98)	27	102 ± 2	(75 – 128)

[a] $p < 0.01$ [b] $p < 0.001$

Rovet *et al.*, 1987. Similar findings have been reported by Rovet *et al.*, who studied intellectual and behavioral characteristics at 1, 2, 3, 4, and 5 years of age of 23 boys and 57 girls with congenital hypothyroidism. The children were

assigned to two groups based on degree of skeletal maturity at the time of diagnosis. Forty-five children with bone age <36 weeks were assigned to the delayed group; 35 with bone age 37 to term were assigned to the nondelayed group. Both groups were treated for congenital hypothyroidism and the initial starting dosages of L-thyroxine for the delayed and nondelayed were similar, 8.1 mg/kg and 7.8 mg/kg, respectively. Although most children with athyrosis were found in the delayed group, the group did not differ in birth weight, hormone levels, or family background. Hormone levels at diagnosis of both groups are shown in Table 12. Tests showed that although children in the delayed group performed within the normal range, their scores were significantly lower than those of the nondelayed group from age 2 years on. Perceptual-motor, visuospatial, and language areas were most affected.

Table 12. Hormone Levels at Diagnosis in Children with Delayed and Nondelayed Skeletal Maturity (Rovet *et al.*, 1987)

	Delayed (n = 45)	**Nondelayed (n = 35)**
	TSH (U/dL)	
Screening	136.1 ± 128.8	130.6 ± 78.6
Confirmation	112.5 ± 119.2	131.9 ± 100.5
	Thyroxine (T4) (µg/dL)	
Confirmation	5.1 ± 4.7	5.5 ± 3.9
1 month	11.0 ± 5.3	10.3 ± 5.7
3 months	12.0 ± 4.5	13.5 ± 3.9
6 months	13.6 ± 2.8	12.6 ± 3.2
9 months	12.4 ± 3.5	14.1 ± 5.3
12 months	12.7 ± 2.7	13.5 ± 2.3

Values represent mean ± standard deviation.

Vermiglio *et al.*, 1990. This study demonstrated that normal euthyroid children born to mothers from severe (area A) and less severe (area B) iodine deficiency regions in northeastern Sicily have a defective visual perceptual integrative motor ability. They studied 719 primary schoolchildren (366 males and 353 females) from these areas ranging from ages 6 to 12 years old (conceived and born between 1975 and 1981). A control group consisted of 370 age-matched schoolchildren from an iodine-sufficient area where rates of goiter were lower (area C). The prevalence of goiter in the schoolchildren of these areas and the daily urinary iodine excretion in the general population between 1976 and 1984 are given in Table 13.

Table 13. Prevalence of Goiter in Schoolchildren and Daily Urinary Iodine Excretion in Adults (1976-1984) in the Study Areas (Vermiglio *et al.*, 1990)

Study area	Total population	Prevalence of goiter in the schoolchildren (%)	Daily urinary iodine excretion (µg/day)[a]
Area A (with endemic cretinism)	7,432	70.3 (708)	24.3 ± 16.4 (55)
Area B (without endemic cretinism)	10,992	45.9 (763)	31.3 ± 18.7 (150)
Area C (control area)	9,730	8.9 (370)	82.4 ± 43.0 (30)

[a]Mean ± standard deviation; the number of observations is given in parentheses.

Variable degrees of thyroid enlargement were found in 205 of the 719 (28.5 percent) children included in the study from areas A and B (area A: 30.4 percent, visible goiter 15.2 percent; area B: 26.5 percent, visible goiter 16.3 percent). Furthermore, defective visual perceptual integrative motor ability (the Bender Gestalt test) was significantly higher in children from area A (14.4 percent) and area B (13.1 percent) than in those from area C (3.5 percent) (Table 14).

Table 14. Number of Defective, Borderline, and Nondefective Schoolchildren as Assessed by the Bender Gestalt Test (Vermiglio *et al.*, 1990)

Performance on Bender[a]	Area A	Area B	Area A+B	Area C
Defective	53 (14.4)	46 (13.1)	99 (13.8)	13 (3.5)
Borderline	57 (15.5)	67 (19.1)	124 (17.2)	14 (3.8)
Nondefective	258 (70.1)	238 (67.8)	496 (69.0)	343 (92.7)
Total	368 (100)	351 (100)	719 (100)	370 (100)

Percent in parentheses.
[a]Performance scores: Defective = below -1 standard deviation from average score of normal children of the same age; Borderline = –1 standard deviation from average score; Nondefective = higher than –1 standard deviation from average score.

The statistical comparisons for the Bender Gestalt Test scores across the different areas were as follows:

Defective:

Area A vs. area B: Chi-square (χ^2) =2.75; p=0.87

Areas A+B vs. area C: χ^2 =36.25; p<0.000001

Borderline:

Area A vs. area B: χ^2 =1.22; p=0.27;

Areas A+B vs. area C: χ^2 =77.55; p<0.000001

Vermiglio *et al.* (1990) also reported higher frequency of neuromuscular and neurosensorial abnormalities among children from areas A and B (a combined overall prevalence of 18.9 percent) compared to those from area C. The Terman Merrill test of general intellectual aptitude was administered to 96 of the 99 "defective" children and 62 of the 124 borderline children from both areas A and B (Table 14). Ninety-one of the 96 "defective" children (94.8 percent) had IQs lower than 90, as did 35 of the 62 borderline (56.4 percent) children (Table 15).

Table 15. Performance on the Terman Merrill Test of General Intellectual Aptitude Administered to Schoolchildren with Defective or Borderline Performance Scores on the Bender Gestalt Test (Vermiglio *et al.*, 1990)

Performance on Bender test	Intelligence Quotient Score		
	< 90	90-95	96-100
Defective (n = 96)	91	5	0
Borderline (n = 62)	35	23	4
Nondefective (n = 12)	0	10	2

Statistical analysis: χ^2 =52.1; p<0.0000005.

Despite the adverse effects described above, the serum T3 and T4 levels of the children from area A and area B were within the normal range. This suggests that serum T3 and T4 are not completely accurate indicators of the neurological damages that may be caused by iodine deficiency.

Tillotson *et al.*, 1994. These authors reported the results of a prospective study of psychological outcomes of 361 children with congenital hypothyroidism after five years of treatment and follow-up. They also selected 315 children as controls, matched for school attended, sex, age (within three months), language spoken at home, and social class defined by occupation of the family breadwinner. The severity of the hypothyroidism was assessed using T4 measurements collected at the time of diagnosis (median age 17 days; range 0-114). The study showed that among children with congenital hypothyroidism and given early treatment, those with plasma T4 concentrations of less than 42.8 nmol/L (3.3 µg/dL) at the time of diagnosis had a global deficit in mean IQ of 10 points, while those with higher T4 levels at the time of diagnosis had no deficit.

Bleichrodt and Born, 1994. These authors performed a meta-analysis on 18 studies of iodine deficiency and mental development. Studies included those with information on the general cognitive functioning of children and adults living in iodine-deficient areas and provided the necessary statistical data. Three studies were excluded from the analysis because the composition of the groups studied was different (they were composed exclusively of school children). In the meta-analysis of the effects of iodine deficiency on cognitive development, a large effect size was found with a d-value of 0.90. This means that the mean scores for the two groups (the iodine-deficient group and the non-iodine-deficient group) were 0.90 of a standard deviation (or 13.5 IQ points) apart.

Pop *et al.*, 1999. Pop *et al.* (1999) reported that low maternal fT4 concentrations in apparently healthy women during early gestation are associated with an increased risk of impaired neurodevelopment in the infant. They studied a group of 291 pregnant women in an iodine-sufficient area (in and around the city of Veldhoven, Netherlands) between January and November, 1994. No women in the study group were receiving antithyroid drugs or thyroid hormones. Maternal fT4, TSH, and thyroid peroxidase antibodies were assessed at 12 and 32 weeks' gestation, and neurodevelopment of 220 healthy children was assessed at 10 months of age. The authors found that children of women with fT4 levels below the 5th (<9.8 pmol/L, n=11) and 10th (<10.4 pmol/L, n=22) percentiles at 12 weeks' gestation had significantly lower scores on the Bayley Psychomotor Developmental Index (PDI) scale at 10 months of age than children of mothers with higher fT4 values. These findings are shown in Table 16. The mean of PDI scores in all subjects was 100, so the decreases seen here represent about a 7-14 percent decrease. The unadjusted odds ratio for impaired psychomotor development (defined as a one standard deviation decrease from the mean) for fT4 in the lower 10th percentile was 3.6 (95% CI, 1.1-12.1). This rose to 5.8 (95% CI, 1.3-12.6) following adjustment for alcohol use, anti-thyroid antibodies, depression, education and other factors.

Although the mean fT4 value for subjects in the lower 10th percentile of fT4 is not given (only the percentile cut-off points are provided), they can be estimated from Table 1 and Figure 2 of the paper. The mean fT4 for subjects in the lower 10th percentile is approximately 9.8 pmol/L compared to a mean fT4 of a little over 13.1 in the remaining subjects. This represents a difference of about 25 percent. Thus, a 25 percent lower maternal fT4 was associated with about a 7 percent decrease in PDI scores in children.

Evidence of a linear association between maternal fT4 and child PDI scores was seen in those children with maternal fT4 levels in the lower 10th percentile ($r = 0.46$, $p = 0.03$). No correlation was found between maternal thyroid hormone levels at 32 weeks' gestation and PDI scores. All children had normal T4 and TSH values. Six of the 22 women with fT4 values in the lower 10th percentile had high levels of anti-thyroid antibodies.

Table 16. Maternal fT4 Levels at 12 Weeks Gestation and PDI Scores in Children at 10 Months of Age (Pop *et al.*, 1999)

Low Maternal fT4 Group[a]	Difference in PDI scores	95% CI
Lower 5th percentile (n = 11)	14.1	5.9-22
Lower 10th percentile (n = 11)	7.4	1.1-13.9

[a] These groups were compared to all the children with higher maternal fT4 levels.

Haddow *et al.*, 1999. This study involved measurements of TSH, fT4, and T4 in 25,216 pregnant women in Maine at 17 weeks of gestation. Three subgroups of women were selected from this large cohort: 47 women with TSH levels in the upper 99.7th percentile, 15 women with TSH levels in the upper 98th to 99.6th percentile, and 124 women with TSH levels below the upper 98th percentile (the "controls"). Measurements of thyroid function of the women in the study are shown in Table 17. Notably, the fT4 and T4 values of many of the women in the high TSH groups are within normal reference ranges. The researchers then administered 15 neuropsychological tests to the children of these women at ages seven to nine years old. The tests included assessment of intelligence, attention, language, reading ability, school performance, and visual-motor performance. The staff giving the tests did not know whether the children's mothers were women with hypothyroidism or control women. They found that the children of the 62 women with high serum TSH concentrations (all those above the 98th percentile) performed less well on all 15 tests. Mean IQ scores, as measured by the Wechsler Intelligence Scale for Children, were 4 points lower in the children of women with high TSH levels compared to the children of the control mothers (103 versus 107, $p = 0.06$). Of the 62 women with elevated TSH levels during pregnancy, 48 were not treated for the condition during the pregnancy. The full-scale IQ scores of their children averaged 7 points lower than those of the 124 matched control children (100 versus 107, $p = 0.005$). Results were controlled for education, maternal age, sampling time, sample storage time, and gender. The effect size seen in this study is similar in magnitude to that seen in Pop *et al.* (1999). That is, a difference in maternal T4 or fT4 of about 25 percent was associated with about a 4-7 percent decrease in IQ.

Sixty-four percent of the women with high TSH levels during pregnancy went on to be diagnosed with clinical hypothyroidism over the next 10 years. None of the children were diagnosed as hypothyroid as newborns. Haddow *et al.* (1999) concluded that even mild and probably asymptomatic hypothyroidism in pregnant women can adversely affect their children's subsequent performance on neuropsychological tests.

Table 17. Measurements of Thyroid Function in the Study Women during Pregnancy (Haddow *et al.*, 1999)[a]

Variable	Hypothyroidism (n = 62)	Controls (n = 124)
Serum TSH (mU/L)	13.2 ± 0.3[b]	1.4 ± 0.2
Serum T4 (µg/dL)	7.4 ± 0.1[b] (95.2 nmol/L)	10.6 ± 0.1 (136.4 nmol/L)
Serum fT4 level (ng/dL)	0.71 ± 0.1[b] (9.1 pmol/L)	0.97 ± 0.07 (12.5 pmol/L)

[a]Values are geometric means ± the logarithmic standard deviation.
[b]$p<0.001$ for the comparison with the control women.

Pop *et al.*, 2003. In another study, Pop *et al.* (2003) reported that a low maternal fT4 during early pregnancy was associated with a delay in infant neurodevelopment. In this study, the researchers followed 115 children and their mothers for two years. Maternal levels of fT4 and TSH were assessed at 12, 24, and 32 weeks of gestation. "Cases" (n = 57) were defined as children of mothers who had fT4 levels in the lower 10th percentile at 12 weeks of gestation and "controls" (n = 58) were defined as children of mothers who had fT4 levels in the upper 50th to 90th percentiles at 12 weeks gestation. Mothers of cases and controls were matched on parity and gravidity. Cases and control families were similar with respect to education, breast feeding, smoking, alcohol use, and income. Mothers with thyroid disease, depression, and TSH levels outside of normal ranges were excluded. Child mental and motor functions were assessed using the Bayley Scales of Infant Development at ages 1 and 2. The results are shown in Table 18. Case children scored 8-10 points lower on the mental and motor scales than control children.

Table 18. Mental and Motor Scale Scores (± Standard Deviation) in Children of Mothers with Low (Cases) and High (Controls) Levels of fT4 at 12 Weeks of Gestation (Pop *et al.*, 2003)

Age	Cases	Controls	Difference (95% CI)	p-value
One year				
Mental score	95 ± 15	105 ± 14	10 (4-16)	0.004
Motor score	91 ± 15	99 ± 14	8 (3-12)	0.02
Two years				
Mental score	98 ± 15	106 ± 14	8 (4-12)	0.02
Motor score	92 ± 16	102 ± 16	10 (6-16)	0.005

All children had normal Apgar scores at birth and normal screening results for congenital hypothyroidism on the seventh postpartum day. Pop *et al.* (2003) observed that children of women who had low fT4 levels during early gestation and who exhibited a further decrease of fT4 during gestation had the lowest mental and motor scores. In contrast, children whose mothers had a low fT4 at 12 weeks gestation, but whose fT4 levels increased during later gestation, did not show any delay in development. Maternal fT4 levels at 24 and 32 weeks gestation were not associated with decreases in childhood motor or mental scores.

The mean fT4 levels at 12 weeks of gestation was 11.5 pmol/l in the case mothers and 17.0 pmol/l in the control mothers (estimated from Figure 2 in Pop *et al.*, 2003), about a 32 percent difference. Thus, a 32 percent difference in fT4 was associated with an 8-10 point drop in mental and motor scores. This is about the same magnitude of effect as seen in Pop *et al.* (1999) and Haddow *et al.* (1999). Importantly, the cut-off point used to define cases (the 10th percentile)

is above the level traditionally used to define low fT4 levels (the 2.5th or 5th percentiles), thus many of the cases had maternal values of fT4 that would traditionally be defined as normal. Figure 3 of Pop *et al.* (2003) presents a scatter plot of maternal fT4 values and childhood mental and motor scores in the case children at 2 years of age. Evidence of a linear relationship is present for both mental scores ($r^2 = 0.13$, $p = 0.006$) and psychomotor scores ($r^2 = 0.23$, $p = 0.001$). These r^2 values suggest that maternal fT4 accounts for a statistically significant fraction of the total variance in these scores.

Klein *et al.*, 2001. In a follow-up investigation, Klein *et al.* (2001) studied serum TSH concentrations of pregnant mothers at a mean of 17 weeks gestation and the standard neuropsychological testing results of their offspring at a mean age of 8 years. They found an inverse correlation between the severity of maternal hypothyroidism and IQs in the offspring. The researchers divided the mothers and their offspring into three groups: group 1, 124 control mothers with TSH concentrations <98th percentile; group 2, 28 mothers with TSH concentrations between the 98th and 99.85th percentile; group 3, 20 mothers with TSH concentrations ≥99.85th percentile. Mothers treated for hypothyroidism during pregnancy were excluded from the study. The mean neuropsychological test score (± standard deviation) for the children of the 124 control mothers was 107 (± 12). Means (and standard deviations) for the children in groups 2 and 3 were 102 (± 15, $p > 0.05$ compared to group 1) and 97 (± 14, $p = 0.003$ compared to group 1), respectively. The incidences of IQs greater than one standard deviation below the control mean were 15 percent, 21 percent, and 50 percent for the children in group 1, group 2, and group 3, respectively. In a related study, the same authors also reported spontaneous abortions and intra-uterine fetal deaths were more than five times as common in the mothers with TSH concentrations above the 98th percentile than in control mothers with TSH concentrations below the 98th percentile.

Kooistra *et al.*, 2006. This study involved the children of 108 pregnant women who had fT4 values below the 10th percentile at 12 weeks gestation ("cases") and 96 pregnant women who had fT4 values in the 50th to 90th percentiles at 12 weeks gestation ("controls"). People with clinical disease were excluded. Case and control mothers were matched on parity and gravidity. Newborn development was assessed at 3 weeks of age using the Neonatal Behavioral Assessment Scale. Mean thyroid hormone levels in the cases and controls are shown in Table 19.

Table 19. Mean (± Standard Deviation) Maternal fT4 and TSH, and the Proportion with Anti-thyroid Antibodies at 12 Weeks Gestation (Kooistra *et al.*, 2006)

	Cases	Controls	p-value
fT4 (pmol/L)	11.4 ± 1.0	17.0 ± 0.9	< 0.001
TSH (mIU/L)	1.6 ± 1.0	1.1 ± 0.8	< 0.001
Anti-thyroid Antibodies	16.7%	4.2%	< 0.01

A statistically significant difference between case and control children was only seen in the orientation scores. In the linear regression analysis with orientation score as the dependent variable, a statistically significant association was seen for case status ($\beta = 0.173$, $p = 0.02$). The researchers also performed a logistic regression analysis where a "low orientation score" was used as the dependent variable. This was defined as subjects who had scores less than one standard deviation below the mean score. The odds ratio for a low score in controls versus cases was 0.17 (95% CI, 0.05 - 0.51). This was adjusted for maternal smoking, alcohol use, gestational age, depression, gender of the child, and maternal education. No difference was seen between case and control maternal fT4 or TSH during the 2nd or 3rd trimester or in the newborns' heel stick T4. No associations were seen between Neonatal Behavioral Assessment Scale scores and TSH or fT4 later in pregnancy.

This study is different from some of the other studies discussed above because the children were very young at the time their cognitive status was assessed. The authors argue that this is an advantage because it limits the impact of external socioeconomic factors that can affect a child's cognitive development as they age. The authors also note a potential major disadvantage: a test given this early may not be predictive of development later in life.

Vermiglio *et al.*, 2004. This was a 10-year prospective study which included 16 healthy women and their offspring from a moderately iodine deficient area (area A, mean urinary iodine levels = 48.1 µg/day) and 11 healthy control women and their offspring from a marginally iodine sufficient area (area B, mean urinary iodine levels = 95.2 µg/day) in Northeastern Sicily. Maternal levels of thyroid hormones were assessed at 8, 13, and 20 weeks of gestation. In the offspring, IQ scores and tests for attention deficit and hyperactivity disorder (ADHD) were done at ages 8-10 years. IQ scores were obtained using the Wechsler Intelligence Scale for Children, 3rd Edition, and tests for ADHD were derived from the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition.

All children were euthyroid at delivery, at ages 18-36 months, and at ages 8-10 years. ADHD was diagnosed in 11 of 16 children from the low iodine area and in none of the 11 children from the moderate iodine area. The mean IQ score in the children from the low iodine area was 18 points lower than the mean score in the

children from the high iodine area (92.1 ± 7.8 versus 110 ± 10, $p < 0.00005$). Maternal fT4, T4, and TSH levels at 8, 13, and 20 weeks were presented graphically and showed that fT4 and T4 levels were roughly 10-20 percent lower for those children from the low iodine area (A) compared to children from the moderate iodine area (B). Eight of the 16 women from the low iodine area had fT4 values that were lower than normal for the gestational week. Seven of these eight gave birth to 8 of the 11 children subsequently diagnosed with ADHD. Only one woman from the control area had a gestational fT4 value outside of normal ranges.

When all children were grouped together, a strong correlation was seen between the child's IQ score and maternal fT4 ($r = 0.56$, $p < 0.005$) and TSH ($r = -0.63$, $p < 0.001$). These results and the graph of these data (Figure 3 in Vermiglio *et al.*, 2004) suggest that the relationship between T4 and IQ extends into the normal ranges of T4.

Bath *et al.*, 2013. In this study, mother-child pairs (n=958) in the Avon Longitudinal Study of Parents and Children in southwest England were used to evaluate the relationship between maternal urinary iodine concentrations measured in the first trimester of pregnancy (median 10 weeks, collected in 1991-92) and the IQ (abbreviated form of the Wechsler Intelligence Scale for Children) and reading ability (Neale Analysis of Reading Ability) of the offspring measured at ages 8 and 9 years. The odds ratio for having a verbal IQ score in the lower quartile in those whose mothers had a urinary iodine to creatinine ratio of <150 µg/g, compared to those whose mothers had a urinary iodine to creatinine ratio of ≥150 µg/g, was 1.58 (95% CI, 1.09-2.30, p=0.02). Corresponding odds ratios were 1.69 (95% CI, 1.15-2.49) for reading accuracy and 1.54 (95% CI, 1.06-2.23) for reading comprehension. Evidence of dose-response trends were seen when subjects were divided into three iodine-creatinine ratio groups. The odds ratios for performance IQ (odds ratio = 1.22; 95% CI, 0.86-1.72) and words read per minute (odds ratio = 1.20; 95% CI, 0.83-1.74) were above 1.0, but not statistically significant. Adjustments for over 20 different potential confounding variables including maternal age, parenting score (a seven factor measure of cognitive stimulation at age 6 months), gender, birth weight, breastfeeding, smoking, alcohol consumption, parental education, and housing status had little impact on most results. Strengths include the longitudinal design, the fairly large sample size, and availability of data on a large number of potential confounders. Potential weaknesses include the possibility that despite the large amount of data on potential confounders, it is still possible that some important determinants of child cognition were not accounted for. This seems unlikely given the fact that odds ratios changed only slightly with the many adjustments that were done. Another potential weakness was the use of a single measurement of urinary iodine to represent long-term iodine status, although this would most likely bias results to the null. Overall, these data provide some evidence that relatively low iodine status during pregnancy can impact the child's cognitive development.

Other studies: Not all studies have found associations between fetal hypothyroidism and impaired brain development. Several studies examined children exposed to antithyroid drugs such as carbimazole, propylthiouracil, or thiamazole *in utero* and did not find an association between the treatment and the later intellectual and somatic development of the children (McCarrol *et al.*, 1976; Burrow *et al.*, 1978; Messer *et al.*, 1990). The statistical power of these studies may be limited since they had relatively small sample sizes and the dosage and timing of the treatment were not known in many cases. In the study reported by Burrow *et al.* (1978), most of the treated children were exposed to propylthiouracil *in utero* during the third trimester, and only four were exposed during the first and second trimester. The studies reported by Burrow *et al.* (1978) and Messer *et al.* (1990) were retrospective studies in which maternal T4 levels during the first and second trimesters were not known. It is possible that the treated women had normal T4 levels during the early part of their pregnancies.

Fenzi *et al.* (1990) conducted neuropsychological assessments on a group of 384 school children (aged 6-14 years) residing in an area of known iodine deficiency (Tuscany, Italy). A group of 352 sex- and age-matched schoolchildren from an iodine sufficient area was used as a control group. Goiter prevalences in the endemic and control areas were 51.9 percent and 5.6 percent, respectively. No statistically significant differences in serum total T4, total T3, TSH levels between the endemic and control areas were found. Serum thyroglobulin values were higher in the iodine-deficient area. Global neuropsychological performance and cognitive levels were similar between a group of 50 schoolchildren from the endemic area and another group of 50 schoolchildren from the control area, matched for age, sex and socioeconomic conditions. However, Fenzi *et al.* (1990) also found that some marginal impairment, with particular regard to motor-perceptual functions, was present in areas of moderate iodine deficiency.

The New England Congenital Hypothyroidism Collaborative Program (1981) found that there was no correlation of eventual IQs with the severity of thyroid dysfunction or with the results of biochemical tests at the time treatment was begun, provided it was begun before clinical hypothyroidism appeared. A diagnosis of hypothyroidism was made when an infant's initial blood concentration of T4 was two or more standard deviations below the mean for newborn infants (6 µg/dL or less) and circulating TSH concentrations were elevated on repeated occasions. Three hundred thirty-six thousand newborn infants in Connecticut, Maine, Massachusetts, New Hampshire, and Rhode Island born between January 1, 1976 and June 30, 1978 were screened. Sixty-three infants were diagnosed with hypothyroidism and treated with L-thyroxine in doses sufficient to maintain circulating T4 concentration between 10 and 14 µg/dL during the first year of life and between 8 and 11 µg/dL thereafter. The control group consisted of 57 euthyroid children who had low T4 and normal TSH concentrations on neonatal screening. The revised Stanford-Binet examination was given to all the test subjects at 3 or 4 years of age. The authors reported that the mean IQ for the hypothyroid infants with adequate thyroid treatment was

106±16 and the mean for the controls was 106±15. They also reported that half of the patients with the lowest IQs (more than one standard deviation below the mean) had normal bone maturation. It is important to note that the results of Pop *et al*. (1999) indicated that it is the low maternal T4 level during early gestation (around week 12) that is associated with impaired neurodevelopment in the infant. It is possible that T4 levels at birth are not a perfectly accurate indicator for thyroid related neurodevelopmental deficiencies occurring in early gestation.

Liu *et al*. (1994) examined the IQs of eight children (Group 1) who were born to mothers that were hypothyroid during the first trimester of pregnancy. Maternal free T4 values at the 5^{th} to 10^{th} gestation weeks ranged from 2.3 to 6.3 pmol/L (normal range, 11.6 to 24.5 pmol/L) in six of the eight cases. In the other two cases, maternal total T4 values were 52.8 and 30.9 nmol/L (normal range, 92.7 to 218.8 nmol/L). TSH levels of the eight mothers at that time ranged from 25 to 190 mU/L (normal range < 5 mU/L). Maternal T4 and TSH levels became normal after T4 supplementation by 13 to 28 weeks of gestation. Seven of the eight children had nine siblings who had not been exposed to maternal hypothyroidism throughout gestation (Group 2); they were used as controls. Ages of the children in groups 1 and 2 at the time of IQ examination were 4 to 10 years in group 1 and 4 to 15 years in group 2. The investigators reported that all children in group 1 showed normal IQs. There was no statistically significant difference in the mean IQ between the children in group 1 who had siblings (112±11) and their siblings in group 2 (106±8). The study is limited by the small sample size. The administration of T4 supplement to hypothyroid mothers at 13 weeks of gestation might have averted adverse neurological development in the fetuses.

Summary of Data on Thyroid Hormones and Childhood Cognitive Development

While not all studies have reported clear links between maternal or neonatal levels of thyroid hormone and the subsequent neurological development of the child, at least five studies have. Studies by Haddow *et al*. (1999), Pop *et al*. (1999, 2003), Kooistra *et al*. (2006), and Vermiglio *et al*. (2004) have all reported statistically significant deficits in measures of childhood cognition and development in groups whose maternal gestational levels of T4 or fT4 include values that have traditionally been considered to be within normal reference ranges. For example, in Kooistra *et al*. (2006), the mean 12-week gestational fT4 in the low fT4 group was 11.4 pmol/L. Since the reference range given by the authors was 8.7-19.6 pmol/L, it is likely that the majority these mothers had fT4 values within the reference range. In addition, all of these studies excluded women with overt clinical thyroid disease, so the effects identified are occurring in the children of women who are asymptomatic. The animal studies by Auso *et al*. (2004), Gilbert and Sui (2008), Lavado-Autric *et al*. (2003), and others support the biologic plausibility that relatively mild decreases in maternal thyroid hormone levels in gestation can cause significant and permanent neurological changes in the offspring.

Some of the effects seen in the human studies are difficult to compare from one study to the next since different outcome measures are used in different studies. Despite this, the magnitudes of the effects seen in these studies seem to be markedly consistent across at least several of them. Table 20 shows the effect sizes in four of these studies. In each, a difference in maternal fT4 or T4 of about 11-32 percent is associated with a decrease in the cognitive development score in the offspring of about 7-16 percent.

Table 20. Comparison of Four Studies of Maternal T4 or fT4 in the First Trimester and Subsequent Child Neurologic Development

	Haddow *et al.*, 1999	Pop *et al.*, 1999	Pop *et al.*, 2003	Vermiglio *et al.*, 2004	Averages
Gestation week	12 weeks	12 weeks	12 weeks	8-13 weeks	
Thyroid measure	T4 (ng/dL)	fT4 (pmol/L)	fT4 (pmol/L)	fT4 (pmol/L)	
Low thyroid group	7.4	9.8[a]	11.5[a]	13.9	
Normal thyroid group	10.6	13.1[a]	17.0[a]	15.7	
Percent difference	30.2%	25.2%	32.4%	11.5%	24.8%
Outcome measure	IQ	PDI	MDI & PDI[b]	IQ	
Percent difference	7%	7%	9%	16%	11%

[a]Approximation based on graphs or other data.
[b]Average of the mean mental developmental index (MDI) and psychomotor developmental index (PDI) scales at ages 1 and 2.

Alterations in Thyroid Hormones and Effects on Serum Lipids and Other Biomarkers of Cardiovascular Disease Risk.

Effects on childhood cognitive development are not the only adverse effects that have been linked with relatively small changes in thyroid hormone levels. The following discussion focuses on the possible cardiovascular effects of relatively minor changes in thyroid hormone levels.

Asvold *et al.*, 2007. This was a cross-sectional population-based study of TSH and serum lipid levels in 30,656 subjects from Norway. All subjects had no known thyroid disease and all had TSH levels within normal reference ranges (0.50 – 3.5 mU/l). The researchers found a linear and statistically significant (p for trend < 0.001) increase in total serum cholesterol, LDL cholesterol, non-HDL cholesterol and triglycerides, and a linear decrease in HDL cholesterol (p for trend < 0.001), with increasing TSH. Results were adjusted for age, smoking, and time since last meal. Adjustments for daily medication use, month of serum collection, diabetes mellitus, heart disease and stroke had no substantial impact on results. Although the changes were associated with very low p-values, the magnitudes of the changes were relatively small. For example, the mean LDL in the lowest TSH group (TSH = 0.50-0.99 mU/l) was 4.11 mmol/L while the mean

LDL in the highest TSH group (3.0-3.5 mU/l) was 4.34 mmol/L, about a 5 percent change. Although this level of change might be considered small on an individual basis, a 5 percent shift in cholesterol levels in a large population could represent a large increase in the population risks of diseases associated with cholesterol (e.g., heart disease and stroke). The results of this study are supported by other smaller studies which also reported similar effects for thyroid hormone levels within normal reference ranges (Pallas *et al.*, 1991; Bakker *et al.*, 2001; Michalopoulou *et al.*, 1998).

Canaris *et al.*, 2000. This was a cross-sectional study of serum lipids, thyroid hormones, and reported history of thyroid disease in 25,862 self-selected people who attended a statewide health fair in Colorado. Subjects were divided into five groups based on their TSH and T4 levels, and mean levels of serum lipids were determined for each group. The TSH and T4 levels used to define these groups and the mean lipid levels seen in each group are shown in Table 21. Statistically significant trends were seen across groups for total cholesterol (p-trend < 0.001), LDL cholesterol (p-trend < 0.001), and triglycerides (p-trend = 0.02), but not for HDL cholesterol. It is unclear whether these results were adjusted for any other variables although the authors did note that levels of estrogen use were similar across all thyroid hormone categories. Although the presence of a linear trend within the euthyroid group was not specifically evaluated, the overall trend across all of the thyroid hormone groups suggests that a trend is likely to occur over the entire range of TSH values.

Table 21. Mean Lipid Levels in Various Thyroid Groups in Canaris *et al.*, 2000

	Group definitions		Cholesterol (mmol/L)			
	TSH (mIU/L)	T4 (nmol/L)	Total	LDL	HDL	TGs
Hypothyroid	> 5.1	< 57.9	6.5	4.4	1.4	2.0
Subclinical hypothyroid	> 5.1	≥ 57.9	5.8	3.8	1.4	1.8
Euthyroid	0.3-5.1	--	5.6	3.6	1.3	1.7
Subclinical hyperthyroid	0.01-<0.3	--	5.4	3.4	1.5	1.6
Hyperthyroid	≤ 0.01	--	5.2	3.4	1.3	1.6

Abbreviations: TGs, triglycerides.

Dullaart *et al.*, 2007. This was a cross-sectional study of carotid artery intima media thickness (IMT) in 44 men and 34 women who all had fT4 (11.0-19.5 pmol/L) and TSH (0.5 mU/L -4.0 mU/L) levels within normal reference ranges. IMT is a subclinical measure of potential atherosclerosis. In multiple linear regression analyses adjusted for age, gender, pulse pressure, body mass index,

and HDL cholesterol, IMT was inversely related to fT4 (β = -0.19, p = 0.046), but not to TSH or the presence of anti-thyroid antibodies.

While several previous studies have reported that overt thyroid disease is associated with increased cardiovascular disease risks (Boelaert and Franklyn, 2005; Vanhaelst *et al*., 1967; Becker, 1985), the findings from this study and the studies of Asvold *et al*. (2007) and Canaris *et al*. (2000), all provide evidence that cardiovascular disease risk is also affected by decreases in thyroid hormone levels within normal reference ranges.

4. TOXICOLOGICAL EFFECTS IN HUMANS

The primary action of perchlorate in the human body is that it blocks iodide uptake in the thyroid gland. The function of the thyroid gland is the production of thyroid hormone. Iodide is a key component in the structure of thyroid hormone, and by blocking its uptake into the thyroid gland, perchlorate can potentially cause a decreased production of thyroid hormone.

As perchlorate competitively blocks iodide from entering the thyroid gland, many of the adverse effects of perchlorate exposure in the low dose range are expected to be similar to those of iodine deficiency. For this reason, an overview of some of the adverse health effects of iodine deficiency was provided in the chapter "Adverse Effects of Thyroid Hormone and Iodine Deficiency."

Developmental and Reproductive Toxicity

Studies of the impacts of perchlorate on thyroid hormone levels in newborns or children are discussed in this section. Impacts in adults, including pregnant women, are discussed in the following section.

Several studies have assessed the association between maternal exposure to perchlorate in drinking water during pregnancy and changes in thyroid hormone levels in newborns. Most of these studies used thyroid hormone levels that were collected as part of state-mandated screening programs for congenital hypothyroidism. Although these programs typically involve measuring thyroid hormone levels at any time in the first two weeks after birth, levels collected in the first 1-2 days after birth may be particularly important for several reasons. First, studies have shown that subtle changes in thyroid hormone levels may have greater impacts on brain development if they occur in the fetal period than if they occur later (i.e., in the newborn or young child) (Pop *et al.*, 2003; Kooistra *et al.*, 2006). Since thyroid hormone levels generally cannot be measured in the fetus during pregnancy in humans, the best practicable way to assess any effect in the fetus caused by perchlorate exposure to the mother during pregnancy would be to measure thyroid hormone levels in the child as soon after birth as possible (e.g., within the first 1-2 days after birth). Second, most of the human studies on newborn thyroid function and maternal perchlorate exposure categorized exposure based on the concentration of perchlorate in the mother's residential drinking water *during* pregnancy, not on the actual perchlorate intake of the newborn *after* birth. This is important since the half-lives of both perchlorate and thyroid hormones in newborns are fairly short (less than 24 hours) (Greer *et al.,* 2002; Van den Hove *et al.*, 1999). As such, any effect that the mother's perchlorate exposure during pregnancy might have on the fetal thyroid should be seen within the first 24 hours after birth (e.g., within the thyroid hormone and perchlorate half-lives). But, they may not be seen at a later time if perchlorate exposure changes at birth. For example, the newborn may be fed an

infant formula with a different perchlorate concentration than that of the drinking water used by the mother during pregnancy. Perchlorate exposure may also change after birth in breast-fed infants if the mother uses water from the hospital or bottled water that has a different perchlorate concentration than the residential water used before birth.

The exposure to the infant might also be affected by the different kinetics of transplacental versus breast milk transfer of perchlorate. Since most of these studies based exposure status solely on the water source used by the mother before birth, any change in exposure in the child after birth could lead to a misclassification of exposure that would bias results towards the null and could cause any true effect to appear to diminish relatively soon after birth. Since the half-life of thyroid hormone in the child is short, this bias would most likely begin to occur within 24 hours after birth and become stronger thereafter. Because of this potential bias, our evaluation of these studies adds an additional emphasis on thyroid hormone measurements collected within the first 24 hours after birth.

Clinical Studies of Developmental and Reproductive Toxicity

Crooks and Wayne (1960) administered potassium perchlorate at 600 to 1,000 mg/day to a group of pregnant women that were suffering from hyperthyroidism and observed a very slightly enlarged thyroid in 1 of the 12 infants born to the mothers. They also reported that the enlarged thyroid returned to normal size in six weeks, and no other abnormalities were observed. Several key parameters were not provided in the paper: detailed dosage information, time of perchlorate treatment in relation to the gestation period, thyroid function of the newborns, and the neurological as well as behavioral development of the offspring. Furthermore, interpretation of the result is made difficult by the fact that the women were suffering from thyrotoxicosis (excess quantities of thyroid hormones).

Epidemiologic Studies of Developmental and Reproductive Toxicity

DHS, 1997. A preliminary health review of a potentially perchlorate-exposed area of Rancho Cordova, CA by the California Department of Health Services (DHS, 1997) included an analysis of several state databases for possible perchlorate-related adverse health effects. Analysis of newborn thyroid hormone data for the period 1985 through 1996 did not indicate a positive correlation between residence in potentially perchlorate-exposed areas and neonatal hypothyroidism. The TSH levels of neonates with initially low T4 levels in the potentially exposed areas were found to be statistically lower than those in the control areas, contrary to what was expected.

Kelsh *et al.*, 2003. This investigation used the California Newborn Screening database to study the thyroid health of newborns whose mothers resided in the city of Redlands, California during the years 1983 through 1997. Perchlorate at variable levels has been detected in groundwater wells in this city. The

outcomes assessed were neonatal primary congenital hypothyroidism (PCH) and elevated neonatal serum levels of TSH (> 25 µU/mL). PCH is a severe condition, usually caused by a missing or partially missing thyroid gland in the child. It is generally associated with very large increases in TSH (e.g., > 25 µU/mL) and often requires treatment with thyroid hormone to prevent severe neurologic and physical growth deficits. TSH measurements were only collected when T4 levels were low (typically below 9 µg/dL or in the lowest five percent of the remaining daily tray samples). PCH was defined as an elevated TSH plus a physician's confirmatory diagnosis. Newborns of San Bernardino and Riverside counties, excluding newborns from Redlands and other communities where perchlorate has been detected, were used as the comparison group. The Colorado River is one of the water sources of Riverside County, so the water serving some of the "unexposed" comparison group may have been contaminated with perchlorate. Perchlorate exposure in the comparison areas would most likely bias any true associations towards the null. There is little information about the perchlorate levels in the drinking water in this area during the study period since the detection limit of perchlorate in water before 1997 was about 400 ppb. In the 2001 and 2002 Consumer Confidence Reports, the City of Redlands reported that the concentrations of perchlorate in its water system ranged from non-detect to 9 ppb, with an average concentration below 1 ppb. However, the California Department of Public Health reported perchlorate levels in Redlands wells in 1997 ranged from 4 ppb to 130 ppb, although it is unknown how much water from the high exposure wells was used for drinking.

Kelsh *et al*. (2003) found no increase in the prevalence of PCH in Redlands newborns over the 15-year study period, although there were only two cases of PCH reported in Redlands during this time. Because there is a normal transient surge in neonatal TSH levels immediately after birth, measuring TSH levels within the first few hours of birth can lead to a high rate of false positives in screening programs for PCH. Because of this, the researchers did further analyses, which excluded subjects who had TSH measurements collected within the first 18 hours of birth. However, as discussed above, measurements collected in the first day after birth may actually be the most relevant, and as discussed below, the post-natal surge in TSH does not necessarily invalidate associations identified between perchlorate and neonatal thyroid hormone levels during this time.

The odds ratio for an elevated TSH for Redlands compared to San Bernardino/Riverside Counties for all subjects (regardless of the age at measurement), and for only those subjects with TSH measurements collected at ≥ 18 hours of age reported by Kelsh *et al.* (2003) were 1.24 (95% CI, 0.89-1.68) and 0.69 (95% CI, 0.27-1.45), respectively. The prevalence ratio for PCH standardized by ethnicity, sex, birth weight, and birth year for Redlands compared to San Bernardino/Riverside Counties was 0.45 (95% CI, 0.06-1.64). The researchers found that Hispanic ethnicity, low and high birth weight, and female sex were risk factors for PCH.

Kelsh *et al.* (2003) did not calculate the odds ratio for having a low T4 (typically defined in this study as a T4 value below 9.0 µg/dL or part of the lowest 5% of the remaining daily tray samples), although this can be estimated using the data in Table 3 of their study. As discussed above, T4 was measured in all newborns, but TSH was only measured if T4 levels were low. Thus, the number of subjects who had "TSH levels screened" represents the number of neonates with low T4 levels. The odds ratio for having a low T4 in Redlands compared to San Bernardino/Riverside Counties was 1.18 (95% CI, 1.13-1.24; $p < 0.0001$). The data used in this calculation is shown in Table 22. This odds ratio is unadjusted. However, it is unlikely that adjusting for age at collection, ethnicity, sex, birth weight, or birth year would have any major impact on this odds ratio since adjusting for these factors had little impact on the TSH odds ratios provided by the authors.

Table 22. Estimated Odds Ratio Calculation for Low T4 in Redlands and in San Bernardino and Riverside Counties Using Data Provided in Kelsh *et al.*, 2003.

Community	Low T4	Normal T4	Total
Redlands	2,081	13,267	15,348
San Bernardino/Riverside	81,401	614,566	695,967
Total	83,482	627,833	711,315

Odds ratio = (2,081/13,267) / (81,401/614,566) = 1.18 (95% CI, 1.13–1.24)

Kelsh *et al.* (2003) also did not report specific results for neonates who had serum TSH measurements collected *before* 18 hours of age. However, data provided in the tables of Kelsh *et al.* (2003) can be used to estimate the odds ratio for having a high TSH level in subjects who had their TSH levels measured during this time. This odds ratio, comparing Redlands to all of San Bernardino/Riverside Counties, was 1.57 (95% CI, 1.14-2.16; $p < 0.0001$). The data used in these calculations are shown in Table 23.

The major strength of the Kelsh *et al.* (2003) study is its large sample size. However, it is limited by the small number of cases of PCH in Redlands, and like most other ecological studies, it was limited by the lack of detailed information on individual exposure (discussed below).

Table 23. Estimated Odds Ratio Calculation for a High Neonatal TSH Level in Subjects with Blood Collected < 18 Hours of Birth Using Data Provided in Kelsh *et al.*, 2003

	TSH Levels		
Area (Perchlorate)	**Elevated[a]**	**Not Elevated**	**Totals**
Redlands (High)	38	4,808	4,846
San Bernardino & Riverside (Low)	1,175	232,990	234,165
Totals	1,213	237,798	239,011

[a]Definitions of "elevated" changed by year, and were between ≥15 and ≥25 µU/mL

Odds ratio = (38/4,808) / (1,175/232,990) = 1.57 (95% CI, 1.14-2.16)

Crump *et al.*, 2000. These investigators studied 162 school-age children (ages 6-8 years old) and 9,784 newborns in three cities in northern Chile that had different concentrations of perchlorate in their drinking water: Taltal (perchlorate concentration, 100 to 120 µg/L), Chañaral (5-7 µg/L), and Antofagasta (non-detectable: <4 µg/L). Approximately 25 separate water sources were sampled in each city. Water samples were taken from water faucets at participating schools, homes of students, and public buildings located near the schools.
The unadjusted mean levels of TSH, T4, fT4, and T3 of the school-age children were very similar across the three cities. Among all the school-age children, there was a small, non-significant increased risk of goiter in Chañaral (26.5 percent) and Taltal (23.3 percent) compared with Antofagasta (17 percent), although this was not seen in analyses confined to life-long residents. The reason for the high prevalence of goiter in the unexposed city of Antofagasta is unknown.

Overall, neonatal TSH levels were similar across the three cities. Adjusted for sex and age, linear regression comparisons of the logarithm (log) of TSH of the newborns by city showed that average logTSH in Taltal was significantly lower than the averages of the other two cities. However, as shown in Table 8 of the Crump *et al.* (2000) paper, TSH levels in those neonates with TSH measured on day 1-2 after birth were higher in Taltal (4.2 µU/mL ± 1.2) than in Antofagasta (3.2 µU/mL ± 3.5) or Chañaral (3.2 µU/mL ± 3.5), although the sample size was small (n = 62).

It should be noted that the iodine levels measured in the schoolchildren in all three study cities were very high. Mean urine iodine levels were 766 µg/L, 614 µg/L, and 756 µg/L for Taltal, Chañaral, and Antofagasta, respectively. These levels are much higher than those in the NHANES III database, where a mean urinary iodine level of 305 µg/L was found for 6-11 year old children in the U.S. The high urinary iodine levels and high prevalence of goiter in this study make it difficult to interpret the relevance of its findings to children in California, where

rates of goiter are much less and moderate iodine deficiency (a potential susceptibility factor) is likely much more common.

Crump *et al*. (2000) found that schoolchildren with lifelong residence in Taltal were five times more likely to have a self-reported family history of thyroid disease than schoolchildren with lifelong residence in Antofagasta. These results were adjusted for age, sex, and urinary iodine (Table 24). Chañaral children had no increased prevalence of self-reported family history of thyroid disease. Families of 19 out of 61 (31 percent) children in Taltal were reported to have some history of thyroid disease. Twelve of these families reported having a single relative (usually a mother or grandmother) with goiter, hypothyroidism, or unspecified thyroid disease; and seven reported having two or more relatives with thyroid disease. The reason why there was evidence of perchlorate-related thyroid effects in older relatives, but not in the children themselves, is unknown. The authors note that the reports on familial history of thyroid issues were not verified and recall bias is possible. They also speculated that this finding might be related to the major changes in average iodine intakes that have occurred in Chile over the last several decades. Iodized salt was introduced to this region in the late 1970's, and average urinary iodine levels in Chile have risen dramatically since that time. For example, according to the International Council for Control of Iodine Deficiency Disorders, average urinary iodine levels in Chile rose from 109 µg/g creatinine in 1982 to 1,191 µg/g creatinine in 2001 (ICCIDD, 2009). It is possible that the elevated odds ratio for a family history of thyroid disease reflects effects that occurred several decades ago when intakes of iodine were low and this low iodine caused some people to be especially susceptible to perchlorate. It is also possible now that iodine levels are much higher, these high levels are protective, and the children and other members of this community are now much less susceptible to perchlorate.

Table 24. Odds Ratios for the Association between Self-Reported Family History of Thyroid Disease[a] among Schoolchildren and City of Residence[b] (Crump *et al*., 2000)

	Schoolchildren with less than lifelong residence (n=162)		Schoolchildren with lifelong residence (n=127)	
City	**Odds ratio**	**95% CI**	**Odds ratio**	**95% CI**
Antofagasta	1.00	-	1.00	-
Chañaral	0.89	0.25-3.19	1.04	0.21-5.09
Taltal	3.35	1.19-9.38	4.97	1.29-19.17

[a]Direct relative (parent, sibling, grandparent, great-grandparent, aunt, uncle, or cousin) with history of goiter, hypothyroidism, or subtotal thyroidectomy.
[b]Adjusted for age, sex, and urinary iodine; excluded one child with autoimmune hypothyroidism.

Assuming the level of perchlorate contamination of the city of Taltal has not changed significantly in the last few decades, a LOAEL of 100 µg/L for familial

thyroid problems can be identified from Crump *et al.* (2000). Applying the default values of 2 L/day for drinking water consumption and 70 kg for an adult body weight, the LOAEL is equivalent to an intake of 3 µg/kg-day from drinking water alone.

Lamm and Doemland, 1999. These authors identified six counties in California (Los Angeles, Orange, Riverside, Sacramento, San Bernardino, and San Diego) and one county in Nevada (Clark) that have had detectable levels of perchlorate (4 to 16 µg/L) in at least some of their drinking water sources. They then compared the rates of primary congenital hypothyroidism (PCH) in these seven counties with overall state rates. All infants were screened by their serum T4 levels, and those with a low T4 (i.e., less than the 10th percentile) were further screened for high TSH levels. An infant was considered to be potentially congenitally hypothyroid if the serum TSH was $\geq$ 25 µU/mL. Infants with these high TSH values were then evaluated by a physician to confirm whether or not they had PCH.

County- and ethnicity-specific data for the two states were obtained for the years 1996 and 1997. Within the seven counties, nearly 700,000 newborns were screened. In all, 249 cases of PCH were identified, where 243 were expected based on the state incidence rate, for an overall risk ratio of 1.0 (95% CI, 0.9-1.2). The risk ratios for the individual counties ranged between 0.6 and 1.1. Out of the 36,016 newborns screened in Clark County (Nevada) between 1996 and 1997, seven cases were observed and 8.3 cases were expected. The risk ratio was 0.8 (95% CI, 0.34-1.74). Based on these results, Lamm and Doemland (1999) concluded that the study did not indicate an increase in the incidence of PCH in those counties with detectable perchlorate levels. Results were not adjusted for several variables related to thyroid hormone levels such as age, gender, or iodine intake, although there is no evidence these factors were related to perchlorate exposure and caused important confounding. Perhaps more importantly, although Clark County of Nevada obtained nearly all of its drinking water from Lake Mead, which is known to be contaminated with perchlorate, the six California counties obtained their drinking water from multiple sources, many of which were not contaminated with perchlorate. Because of this, there was likely significant misclassification of exposure for the California counties. Misclassification could also occur if there were errors in the county to which subjects were assigned, although there is no evidence that this would result in major bias, and bias from this source seems unlikely given the very large size of most of the exposed counties. Importantly, errors in misclassifying exposure would most likely be non-differential and most likely cause bias towards the null. Finally, PCH is a very serious disease, usually requiring treatment with thyroid hormone, and it is generally associated with large increases in TSH. As discussed in subsequent sections, much smaller changes in thyroid hormone levels may also be associated with significant health outcomes, and these more subtle effects would probably be missed in a study that solely focused on physician-diagnosed cases of PCH.

Li *et al.*, 2000a. In a related study, Li *et al.* (2000a) compared serum T4 levels of newborns (collected 1 to 4 days after birth) from the city of Las Vegas, Clark County, Nevada, which has perchlorate in its drinking water, to those from the city of Reno, Nevada, which does not (detection limit, 4 µg/L). A total of 17,308 newborns from Las Vegas and 5,882 newborns from Reno born from April 1998 through June 1999 were included in the study. During the study period, monthly drinking water perchlorate levels for Las Vegas ranged from non-detectable to 15 µg/L. Perchlorate was not detected in the Las Vegas water supply in 8 of the 15 months covered by the study, which the authors suggest may be due to the changing conditions of the water supply to this city. Separate analyses were done to evaluate births in the seven months when perchlorate was detected.

Overall, Li *et al.* (2000a) reported no differences in mean T4 levels (approximately 17 µg/dL) between the two cities ($p = 0.41$), including analyses involving those months where perchlorate was detectable in Las Vegas drinking water (shown in their Figure 1, no p-value given). Specific analyses stratified by age at the time T4 was measured were not presented in detail but are shown in Figure 3 of their paper. Based on this figure it appears that among infants who had their T4 levels collected on day one after birth, the mean T4 level in Las Vegas was about 4 µg/dL (about 22 percent) lower than the mean T4 in Reno.

Li *et al.* (2000a) used the monthly perchlorate measurements in Las Vegas drinking water to estimate the cumulative perchlorate exposure for each newborn during the first three months of pregnancy and for all nine months of pregnancy. Cumulative exposures in Las Vegas ranged from 9 ppb-months to 83 ppb-months; the Reno newborns during this period were presumed to have had no drinking water-related prenatal exposure. In linear regression analyses involving T4 levels collected on all days after birth (not just day one), no association was found between cumulative perchlorate exposure and mean neonatal T4 levels (regression coefficient (β) = -0.0003; $R^2 = 0.002$). Exposure assessment in this study was ecologic and information on whether or not the mothers or infants consumed water from public supplies, or how much they consumed is unknown. As discussed below, this would most likely cause bias towards finding no effect. Misclassification of true long-term thyroid hormone status could also have caused some bias, but again, this would most likely be non-differential and thus most likely cause bias toward finding no effect (also discussed below).

Li *et al.*, 2000b. Li *et al.* (2000b) studied neonatal blood TSH levels sampled between December 1998 and October 1999 in Las Vegas (up to 15 ppb perchlorate in drinking water) and Reno (perchlorate below the detection level of 4 ppb). Serum TSH levels were measured in all neonates who had T4 measurements below the 10^{th} percentile in each daily batch of T4 samples (measured in the first 30 days of life). TSH measurements collected on the first day after birth were excluded. (As discussed above, associations between maternal perchlorate exposures and neonatal thyroid hormone levels are probably best evaluated using TSH measurements taken within the first 24 hours after birth.) In addition, only neonates with birth weights of 2.5 – 4.5 kg were

included. The authors found that neonatal TSH levels were not significantly different between Reno and Las Vegas. Mean TSH values in Las Vegas and Reno were 11.5 µIU/mL (± 1.3) and 12.5 µIU/mL (± 1.3), respectively. The TSH regression coefficient adjusted for age and sex comparing Las Vegas to Reno was -0.0004 (95% CI, -0.0241– 0.0233; p=0.973). Several factors could have caused at least some bias towards finding no effect, including the lack of control of birth weight and ethnic origin, the use of broad categories to control for age at TSH collection (2-7 and 8-30 days), the small sample size, and perhaps most importantly, misclassification of exposure and effect and the exclusion of subjects who had TSH measurements at age < 24 hours.

Brechner *et al.*, 2000. This study identified an association between low-level perchlorate exposure in maternal drinking water and serum TSH levels in newborns. As in the studies discussed above, T4 was measured in all newborns, but TSH was only measured in newborns who had low T4 levels. The investigators compared serum TSH levels in newborns from Yuma, a city that obtains its public drinking water entirely from the Colorado River below Lake Mead, with TSH levels in newborns from Flagstaff, a city that obtains none of its public drinking water from the Colorado River below Lake Mead. Although Lake Mead was known to have perchlorate contamination, no useful water monitoring data were available for Yuma and Flagstaff during the study period (between 1994 and 1997) because the detection limit of perchlorate in water was 400 ppb during that time. In March 1997, the detection limit of perchlorate was improved to approximately 4 ppb. In August 1999, U.S. EPA reported that perchlorate levels in Yuma were about 6 ppb in both raw water and finished drinking water (Brechner *et al.,* 2000).

In unadjusted analyses, Brechner *et al.* (2000) found that median newborn TSH levels in Yuma were significantly higher than in Flagstaff (19.9 vs. 13.4 mU/L). The odds ratio for having a low T4 (and thus being screened for TSH) were not presented by the authors but can be estimated using the data they present in Figure 1 of their study. This odds ratio, comparing Yuma to Flagstaff, was elevated (1.19; 95% CI, 1.07-1.33; p = 0.006). The data used to estimate this odds ratio are shown in Table 25. It should be noted that this odds ratio is not adjusted for age or ethnicity. Four cases of congenital hypothyroidism were reported in Yuma but none in Flagstaff. Because of a normal surge in TSH that occurs soon after birth, a major factor influencing newborn TSH levels is the time (after birth) at which the TSH blood samples are collected. This time was significantly earlier in Yuma than in Flagstaff, and this may have caused some of the increase in TSH levels seen in Yuma compared to Flagstaff. However, according to the authors, the difference in mean TSH levels between Yuma and Flagstaff remained after adjusting for age in days at measurement, gender, and race/ethnicity (p = 0.009) (Brechner *et al.*, 2001). Although the effect size of the adjusted results was not reported, median TSH levels in the two cities stratified by age at measurement are presented. Using the data provided in Table 2 of their article, it can be seen that median TSH levels are greater in Yuma than in Flagstaff on most days of age, with the greatest difference seen on days 0-2 of

age (shown in Table 26). The interpretation of this study is complicated by the fact that TSH levels were only measured in samples with low T4 measurements (discussed below). In addition, this study did not adjust for birth weight or gestational age. The difference in altitude between the two cities has also been cited as a possible bias but it is not clear that this potential confounder would be strong enough to cause the results observed. In fact, several studies suggest the opposite: that high altitudes actually decrease thyroxine levels and have little to no effect on TSH levels (Kotchen *et al.,* 1973; Sawhney and Malhotra, 1991; Richalet *et al.,* 2010).

Table 25. Estimated Odds Ratio for Having Low T4 Using Data Provided in Brechner *et al.*, 2000.

	Low T4		
	Yes	**No**	**Total**
Yuma	1,291	6,308	7,599
Flagstaff	519	3,020	3,539

Odds ratio = (1,291/6,308) / (519/3,020) = 1.19 (95% CI, 1.07-1.33)

Table 26. Median TSH Levels in Yuma and Flagstaff Stratified by Day of Blood Collection (Brechner *et al.*, 2000)

Flagstaff				Yuma			
Days	**N**	**%**	**TSH**	**N**	**%**	**TSH**	**Difference[a]**
0	14	3.2%	24.0	121	11.0%	30.4	6.4
1	122	27.5%	22.0	531	48.3%	25.2	3.2
2	25	5.6%	13.4	116	10.6%	16.5	3.1
3	24	5.4%	11.5	21	1.9%	13.8	2.3
4	15	3.4%	12.3	17	1.5%	12.3	-0.1
5	243	54.9%	10.6	293	26.7%	11.4	0.8
Total	443	100.0%	14.5	1099	100.0%	20.8	6.3

[a]Median TSH in Yuma minus median TSH in Flagstaff.

Buffler *et al.*, 2006. This study was an ecologic analysis comparing neonatal TSH levels in California communities with perchlorate concentrations above 5 µg/L to those in communities with no known drinking water perchlorate measurements above 5 µg/L. Perchlorate levels in community water sources were obtained for the years 1997 and 1998 from the California Drinking Water Program and used to estimate weighted average perchlorate concentrations in community water. TSH levels among 342,257 California newborns screened in 1998 were obtained from the California Department of Health Services (now the California Department of Public Health). The major outcomes assessed in this study were primary congenital hypothyroidism (PCH) and the elevations in TSH typically used to screen for this disorder (i.e., a TSH > 25 µU/mL collected more

than 24 hours after birth). As discussed for the Kelsh *et al.* (2003) study above, PCH was defined as a TSH level > 25 µU/mL and a physician's confirmatory diagnosis. Subjects who were screened before 24 hours of age were excluded from the analyses by the authors because the normal physiologic post-natal surge of TSH that occurs during this period can increase the rate of false positives when screening for PCH.

Overall, Buffler *et al.* (2006) reported an adjusted odds ratio for having TSH > 25 µU/mL of 0.73 (95% CI, 0.40-1.23) comparing the high to low perchlorate communities. The corresponding odds ratio for PCH was 0.71 (95% CI, 0.40-1.19).

As discussed above, although TSH measurements collected within the first 24 hours of birth may not be the most appropriate for screening for PCH, levels collected during this time may be the most relevant for assessing associations between maternal drinking water perchlorate concentrations and changes in neonatal thyroid hormone levels that are less severe than those typically seen with PCH. The odds ratio for all subjects (those with TSH measured < 24 hours of age combined with those with TSH measurements at ≥ 24 hours of age) were not reported by the authors but can be estimated from the data given in Table 1 of Buffler *et al.* (2006). The unadjusted OR for high TSH comparing communities with perchlorate concentrations above and below 5 µg/L in all subjects regardless of the age of measurement was 1.59 (95% CI, 1.33-1.91). The data used in these calculations are presented in Table 27. Again, this odds ratio was not reported by the study authors, and it is an unadjusted odds ratio.

Table 27. Data for Estimated Unadjusted Odds Ratio Calculations for All Subjects in Buffler *et al.* (2006)

	TSH levels		
Perchlorate	**Elevated**	**Normal**	**Totals**
> 5 µg/L	147	50,179	50,326
< 5 µg/L	537	291,394	291,931
Totals	684	341,573	342,257

Odds ratio = (147/50,179) / (537/291,394) = 1.59 (95% CI, 1.33-1.91)

Given the normal TSH surge that occurs in the first 24 hours after birth, OEHHA evaluated the possibility that this elevated odds ratio could be due to earlier TSH testing in the communities with perchlorate > 5 µg/L. An estimate of the percentage of neonates with TSH measurements before and after 24 hours can be obtained by subtracting the number of TSH levels measured at ≥ 24 hours (given in Buffler *et al.*, 2006, Table 4) from the total number of TSH measurements (at any age) (given in Buffler *et al.*, 2006, Table 1). These data are shown in Table 28 below. (These are estimates since Buffler *et al.*, 2006, Table 1 appears to include all subjects whereas Buffler *et al.*, 2006, Table 4

appears to only include subjects who have all of the data on the co-variates used in their adjusted analyses.)

Table 28. Subjects with TSH Measurements before and after 24 Hours of Birth (Buffler *et al.*, 2006)

	Perchlorate	
	≤ 5 µg/L	> 5 µg/L
Total subjects (Table 1)	291,931	50,326
High TSH (Table 1)	537	147
Total > 24 hours (Table 4)	185,528	29,114
Percent	63.6%	57.9%
High TSH (Table 3)	124	15
Percent with high TSH	0.067%	0.052%
Total < 24 hours (calculated)	106,403	21,212
Percent	36.4%	42.1%
High TSH (Table 3)	413	132
Percent with high TSH	0.39%	0.62%

Based on these numbers, the percentage of all neonates with TSH measurements collected within the first 24 hours of birth was greater in the high perchlorate communities than in the low perchlorate communities (42.1 versus 36.4 percent). Importantly though, when analyses are confined to only those subjects with TSH measurements collected at < 24 hours of age, the unadjusted odds ratio for high TSH comparing communities with and without perchlorate > 5 µg/L remained elevated (OR = 1.60; 95% CI, 1.32-1.94). If age at measurement were an important confounder, the expected odds ratio would be near 1.0 after stratifying by age. It is unlikely that the entire 60 percent increase in risk would go away with an even more detailed stratification or adjustment by age at sample collection.

Steinmaus *et al.*, 2010. Individual data were obtained from the Buffler *et al.* (2006) study, and analysis of these confirmed the elevated odds ratios discussed above. For example, the odds ratio for TSH > 25 µU/mL within the first 24 hours of birth was 1.53 ($p < 0.0001$; 95% CI, 1.24-1.89). For TSH levels measured more than 24 hours after birth, the odds ratio for TSH > 25 µU/mL was similar to that reported in Buffler *et al.* (2006). However, a TSH level of 25 µU/mL was the 99.99th percentile of all TSH levels in this age stratum and there were very few exposed cases (n = 13). Because significant neurologic effects have been seen with smaller changes in thyroid hormones (Pop *et al.*, 1999, 2003; Haddow *et al.*, 1999; Klein *et al.*, 2001; Kooistra *et al.*, 2006; Vermiglio *et al.*, 2004), lower TSH cut-off points were also used to define "high" TSH in this paper. When this was done, elevated odds ratios for high TSH were seen both in infants in whom TSH measurements were collected before 24 hours of age and in infants in whom TSH measurements were collected after 24 hours of age. For example, the odds

ratio for having a TSH level above the 95th percentile in samples collected after 24 hours of age comparing perchlorate exposed and unexposed communities was 1.27 ($p < 0.0001$; 95% CI, 1.22-1.33). This study only evaluated TSH levels and it is currently unknown whether the effects seen here cause actual impacts on health and development. These analyses adjusted for age of sample collection, gender, mother's age, per capita income, race/ethnicity, birth weight, and feeding type (breast milk vs. formula), none of which had substantial effects on results. For example, the adjusted and unadjusted ORs for having a TSH level of 25 µU/mL or greater for collection ages less than 24 hours were 1.53 and 1.52, respectively.

The authors of the Steinmaus *et al.* (2010) paper considered analyzing TSH concentrations and community perchlorate concentrations as continuous variables. But, because of the extensively overlapping and continually changing water sources in many parts of California, assigning a single perchlorate concentration to each individual would have introduced considerable misclassification. This would have introduced particularly strong bias in those subjects in the upper ranges of community perchlorate concentration. Instead, communities (and the subjects who lived in those communities) were divided into two groups based on whether or not it was likely the sources of their residential drinking water had perchlorate concentrations greater or less than 5 ppb. Some exposure misclassification was still likely with this type of categorization. However, since the misclassification was most likely non-differential, the bias would likely be in the direction of the null, not in the direction of finding false positive associations.

Li *et al.*, 2001. This study was an ecologic analysis of various thyroid diseases comparing two counties in Nevada: Clark County, where average water perchlorate levels of around 0-14 ppb were reported, and Washoe County which has not had detectable levels of perchlorate in its major drinking water supplies. The largest city in Washoe County is Reno and the largest city in Clark County is Las Vegas. Relative risks for 6 of the 8 diseases assessed comparing Clark County to Washoe County were above 1.0 (although none were statistically significant) including goiter (RR = 1.24), nodular goiter (RR =1.45), thyroiditis (RR=1.69), and other thyroid conditions (RR=1.89). Relative risks for congenital and acquired hypothyroidism were 0.60 and 1.01 respectively. Disease rates were based on Medicaid records which could be a very insensitive marker of the true rates of these diseases since only a fraction of the people in these counties are on Medicaid rolls.

Chang *et al.*, 2003. In a similar study comparing Clark County (known to have elevated perchlorate levels in its drinking water) to the rest of Nevada, no differences were seen in the rates of pediatric neurobehavioral diseases including autism and attention deficit-hyperactivity disorder (ADHD) assessed using Medicaid records. As stated by the authors, "Perchlorate levels in drinking water were measured in Nevada waters following the 1997 detection of perchlorate in the Lower Colorado River with the newly refined perchlorate

assay. The only public water system found to contain perchlorate was that of the Southern Nevada Water Authority (SNWA) that obtained its water from Las Vegas Bay and distributed it to about 96% of Clark County, including the city of Las Vegas. Perchlorate has not been detected in the public water supply of Reno, of Washoe County, or elsewhere in the state of Nevada. The perchlorate content of the raw and finished waters of SNWA have been measured at least monthly, and at times weekly, since July 1997. Perchlorate levels in 149 finished water samples taken between July 1997 and May 2002 had a mean of 10.9 ppb (SD ± 3.9; median = 10.5 ppb; range = nondetect to 23.8 ppb)." Information on the frequency of neurobehavioral diseases in Nevada youths under 18 years old came from the service records of the Nevada Medicaid program for the years 1996–2000. Patients were defined as those under age 18 who were diagnosed with or treated for either ADHD (ICD9 314) or autism (ICD9 299). The "disease incidence" in Clark County and the rest of Nevada was defined as the average annual number of new cases in Medicaid youths seen or treated in each area divided by the number of Medicaid-eligible youths in that area, in the midpoint of 1998. These unadjusted "disease incidences" were then compared, although the results of formal statistical significance testing are not provided. As discussed in many of the other studies reviewed in this section, and reviewed below, results might have been affected by exposure and outcome misclassification or confounding, although too few data are provided to quantitatively evaluate the extent of these issues for this study. Also, no difference was seen in comparisons of 4th grade performance results, although the methods used in this study to assess both exposure and outcome are likely too inaccurate to identify subtle or even moderate effects.

Tèllez Tèllez *et al.*, 2005. Neonatal and maternal thyroid function was assessed in subjects from the same three cities in northern Chile used in Crump *et al.* (2000). These cities (and their mean perchlorate levels in drinking water) were Taltal (100-120 µg/L), Chañaral (5-7 µg/L), and Antofagasta (non-detectable: <4 µg/L). No clear difference was seen in maternal thyroid hormone levels between the three cities (discussed in a subsequent section). In addition, no differences were seen across cities in mean neonatal cord blood fT4 or TSH. Interestingly, 72.7 percent of the births in the high exposure city were males (compared to 49 percent in the low exposure city), and 57 percent of the births from the high exposure city were done by cesarean section (compared to 39 percent in the low exposure city). The reasons for the unusually high proportion of males and the unusually high rate of cesarean-sections in Taltal are unknown.

Mean concentrations of perchlorate in breast milk were similar in the high and low exposure cities (95.6 µg/L versus 81.6 µg/L), although these were highly variable within a city and the median levels were markedly different across cities (< 4 in Antofagasta and 104 µg/L in Taltal). No association was seen between breast milk iodine and perchlorate concentrations. Mean urinary iodine levels in the women were greater than 300 µg/L in all three cities, suggesting that very few women had low iodine intakes. As discussed below, relatively high iodine intakes may help prevent the thyroidal effects of perchlorate. The mean number

of cigarettes smoked per week (0.52 for the 62 women in Taltal) suggested that few if any women were moderate or heavy smokers. In addition, differences in urinary levels of perchlorate were not as great as might be expected based on the perchlorate concentrations reported for the drinking water of each city. For example, maternal urine perchlorate concentrations measured during the post-partum visit for the low, medium, and high exposure cities were 22.3, 17.5, and 49.1 µg/L, respectively, although these measurements were only done in a fraction of the women in the study. A graphical display of the urinary perchlorate levels from all three cities shows a marked overlap across cities. Part of this may have been due to the fact that a large percentage of the women (45 percent) from the high exposure city of Taltal went to the low exposure city of Antofagasta to give birth. Taltal (population about 10,000) is fairly remote and is about 200 miles away from the much larger city of Antofagasta (population about 250,000). Part of it may have been due to exposure from foods or some other unknown source in Antofagasta. Regardless of the cause, the lack of a large contrast in exposure between the subjects from each of the cities probably decreased the likelihood that true associations, if present, could be found.

Amatai *et al.*, 2007. T4 values were measured in newborns in the neighboring cities of Ramat Hasharon and Hertzlia, Israel, whose mothers resided in areas where drinking water had perchlorate concentrations that were very high (340 µg/L, n = 97), high (42-94 µg/L, n = 216), and low (< 3 µg/L, n = 843). The high perchlorate concentrations were found in wells near a military plant. Heel-stick T4 values were measured in all newborns in these communities as part of the national screening program, and were done at 36-48 hours after birth in >90 percent of all newborns. Mothers also completed a questionnaire asking whether they drank tap water, filtered water, or bottled water during their pregnancy.

The mean T4 values in the very high, high, and low perchlorate areas (in µg/dL) were 13.93 (± 3.8), 13.91 (± 3.4), and 13.98 (± 3.5), showing no differences between the exposure areas. It is unclear if these means were adjusted for other factors associated with neonatal T4 levels including gender or the age of the child when the heel stick was taken. No association was seen with neonatal T4 and maternal age, birth weight, gestational age, or sex. No difference was seen in mean T4 values in the analysis confined to only the children of exposed women who reportedly drank tap water during pregnancy, although this included less than 30 percent (n = 93) of the women from the very high and high exposure areas.

Serum perchlorate levels were reported in this study on a small number of people who lived in the study areas and who were proxy donors (i.e., blood bank donors who were not involved in the actual study). Mean serum perchlorate levels (in µg/L) in the very high, high, and low perchlorate areas in these subjects were 5.99 (± 3.89, n = 4), 1.19 (± 1.37, n = 19), and 0.44 (± 0.55, n =14). As seen in Figure 3 of this paper, and in the reported standard deviations, there was considerable overlap in serum perchlorate among the three exposure categories. Serum iodine levels were also measured in the proxy donors. Serum iodine

levels were higher in proxy subjects from the very high/high exposure areas compared to the low exposure area (3.10 µg/L ± 1.25 versus 2.24 µg/L ± 0.85; p = 0.031).

The strengths of this study are its collection of at least some individual data on exposure (i.e., the source of drinking water during pregnancy) and the presumably large contrast in perchlorate exposure. Urinary perchlorate levels would have likely provided a better indication of true exposure but were not measured. Other weaknesses are the lack of information on adjustments for potential confounders, the lack of individual data on smoking and iodine, and the relatively small number of women from the exposed areas who drank tap water during pregnancy. In addition, the authors reported that >90 percent of infants in these areas had their blood sampling at 36-48 hours after birth, suggesting that very few (probably < 4) of the highly exposed study infants had thyroid hormone measurements within the first 24 hours of birth. As discussed above, since the half-life of perchlorate and thyroid hormones is relatively short, this may have limited the ability of this study to find an association between maternal perchlorate exposure during pregnancy and neonatal thyroid hormone levels.

Blount *et al.*, 2009. Perchlorate, nitrate, thiocyanate, and iodine were measured in maternal urine (n=34), amniotic fluid (n=130), cord blood (n=126), and maternal serum (n=132) in mother-offspring pairs from New Jersey. Only subjects scheduled for elective cesarean section were included, and maternal blood and urine were collected within one hour before the surgery. Correlations between the various exposure parameters, as well as associations between perchlorate concentrations in cord blood and birth weight, length, and head circumference, were assessed. Correlations between perchlorate concentrations in maternal urine and concentrations in maternal blood and cord blood were low (-0.10 and 0.20, respectively). Clear associations between concentrations of cord blood perchlorate and birth weight, length, and head circumference were not seen. Because the sample size was relatively small, only very large changes in birth weight, head circumference, and birth length would be detectable with sufficient statistical power. In addition, these outcomes are indicative of effects that are likely much more severe than would be expected from the fairly low perchlorate exposures measured in this study (median urine perchlorate = 2.76 ug/L; 90^{th} percentile = 4.35 ug/L). Finally, urine, rather than blood, is the most common metric used to assess perchlorate exposure, but urine perchlorate was only measured in 34 pregnant women and analyses of associations between maternal urinary perchlorate and fetal birth weight, head circumference, and birth length were not presented.

Cao *et al.*, 2010. Urinary concentrations of perchlorate, nitrate, iodine, thiocyanate, T4 and TSH were measured in 92 full term infants from Pennsylvania. In analyses adjusted for age, sex, and body mass index, increasing urinary perchlorate concentrations were associated with increasing urinary TSH concentrations, but only in children with low urinary iodine. The adjusted regression coefficient between the logarithm of urinary perchlorate and

logarithm of urinary TSH was 0.10 (95% CI, 0.01- 0.19) in children with urinary iodine levels < 100 µg/L and –0.04 (95% CI, –0.12-0.04) in children with higher iodine levels. Increasing urinary concentrations of perchlorate, nitrate, and thiocyanate were also associated with higher urinary T4. Both urinary levels of thyroid hormones and urinary levels of perchlorate (and other analytes) were "adjusted" for urine dilution by dividing their values by the subject's urinary creatinine concentrations. The use of urinary creatinine on both sides of the mixed model analyses (i.e., as part of the dependent variable and as part of the independent variable) may have led to the positive correlations identified in this study, making these results difficult to interpret.

Summary of Studies of Perchlorate and Infant Thyroid Hormone Levels

Table 29 summarizes data from the most relevant studies of perchlorate exposure and newborn thyroid hormone levels. In several studies, the authors did not specifically present results for the early newborn period, but provided data that OEHHA used to perform its own evaluation of possible associations for this period. These are clearly marked in Table 29 under the heading "Source of data and results." It should be noted that the data points calculated by OEHHA are not based on the original study authors' conclusions and most represent unadjusted estimates. Any conclusions drawn from this table should be interpreted in light of these facts. Table 30 lists the studies that were excluded from Table 29, with reasons for their exclusion. The Li *et al.* (2000) and Amatai *et al.* (2007) studies are excluded from this table because they did not include a substantial portion of subjects who had thyroid hormone levels measured within the first 24-36 hours after birth. As discussed above, this period is likely the most relevant time frame for assessing the effects related to maternal exposures during pregnancy. Tèllez Tèllez *et al.* (2005) is excluded from the table because 45 percent of the newborns from the exposed city were born in the unexposed city and therefore were probably not exposed at the time of birth. The Tèllez Tèllez *et al.* (2005) study is also inconsistent with the other studies in Table 29 because the very high iodine levels in this population may have protected the infants in this study from the effects of perchlorate and, more importantly, because a large fraction of women from the highly exposed town gave birth in the low exposure city. The Buffler *et al.* (2006) study was not included because it used the same data as Steinmaus *et al.* (2010) but did not focus on newborns.

As seen in Table 29, at least some evidence of an association was seen with perchlorate in each of the five data sources that included information on newborn thyroid hormone levels. Several aspects of these findings provide evidence that they represent real effects. First, despite major differences in study populations, study designs, time periods, funding sources, and research groups, these results are markedly consistent across studies. This type of consistency across different studies is one of the major tenets of causal inference (Hill, 1965; Rothman and Greenland, 1998b). Second, several of these results have very low p-values, which means that they are probably not due to chance. Third, these findings are consistent with the known biologic mechanism of perchlorate. That is, these

results show that perchlorate may decrease T4 and increase TSH, both of which are effects that are in the direction expected based on the known mechanism of action of perchlorate.

Several additional issues potentially affect the interpretation of these results and these are discussed in the following sections.

Ecologic assessment of perchlorate exposure: Most of these studies used average perchlorate concentrations in large community drinking water supplies as a surrogate for exposure to the individuals in that community. In all of these studies, the reported perchlorate concentrations were based on a relatively small number of samples. Average perchlorate concentrations were then assigned to individuals without knowledge of whether or not they drank the tap water, how much they drank, or for how long they drank it. In addition, drinking water is not the only source of perchlorate, and some exposure will come from food. Lack of data on other sources of perchlorate would likely cause further misclassification of the study subjects' true perchlorate exposure. Importantly though, study subjects were classified in terms of their perchlorate exposure independently of their thyroid hormone status. Thus, any misclassification of exposure is likely to be independent of thyroid hormone status (i.e., non-differential). This type of non-differential misclassification of exposure will likely bias results towards the null. That is, if an association truly exists, non-differential exposure misclassification will most likely cause the magnitude of the observed association to be less than the magnitude of the true association. It will not likely cause a false association or strengthen an association that is truly weak. There are some rare exceptions to this rule, but these exceptions are not likely applicable to the studies in Table 29 (Rothman and Greenland, 1998a).

Despite this misclassification bias, which was likely present to some degree in every one of the data sources evaluated, OEHHA found evidence of an association in each of the data sources presented in Table 29. If non-differential misclassification of exposure could somehow be corrected for in these studies, the effects found would likely be even greater than those reported.

Table 29. Information on Maternal Perchlorate Exposure during Pregnancy and Thyroid Hormone Levels in Early Newborns

Location and source of data	Exposed (exposure level in water)	Unexposed	Results: Exposed group compared to the unexposed group		Source of data and results	Adjustments, stratifications or exclusions	Summary notes regarding confounding[a] and other related findings	
			T4	TSH				
California	Redlands (9 ppb)	Rest of San Bernardino & Riverside Counties	No data	OR for high TSH = 1.57 (95% CI, 1.14-2.16; p < 0.0001) (Table 23 and page 63)	Calculated by OEHHA using raw data provided in Kelsh *et al.*, 2003	Unadjusted results	Adjustments for birth weight, ethnicity, sex, birth year, age, and multiple births had little effect on the authors' original results.	OR for low T4 = 1.18 (95% CI, 1.13-1.24; p < 0.0001) for all ages (Table 22 and pages 62-63)
California	Exposed communities (> 5 ppb)	Unexposed communities (< 5 ppb)	No data	OR for high TSH = 1.53 (95% CI, 1.24-1.89; p < 0.0001)	Steinmaus *et al.*, 2010	Age, gender, race/ ethnicity, feeding type, birth weight, outliers, household income.	None of these factors except formula feeding had major impacts on results.	
Arizona	Yuma (4-6 ppb)	Flagstaff	No data	Mean TSH = 27% higher (Table 26 for day 0)	Calculated by OEHHA using data and results provided in Brechner *et al.*, 2000	T4 findings based on unadjusted analyses. TSH findings in analyses stratified by age and race/ethnicity.	In follow-up analyses, TSH remained elevated in the exposed town after entering age, race/ethnicity, and sex into the statistical models.	OR for low T4 = 1.19 (95% CI, 1.05-1.33; p = 0.006) for all ages (Table 25 and pages 67-68)

Table 29 (continued). Information on Maternal Perchlorate Exposure during Pregnancy and Thyroid Hormone Levels in Early Newborns

Nevada	Las Vegas (0-9 ppb)	Reno	Mean T4 ≈ 22% lower	No data	Estimated by OEHHA using the data presented in Figure 3 of Li *et al.*, 2000a	Unadjusted result	In the analyses done by the authors, adjustments for sex, birth weight, and age appear to show no major confounding effect.	
Chile	Taltal (100 ppb)	Antofagasta and Chañaral (0-5 ppb)	No data	Mean TSH ≈ 45% higher	Based on the results presented in Table 8 of Crump *et al.*, 2000	Results stratified by age	Median age greater in Taltal than other cities (6.6 vs. 4.1 days). Correcting for this would increase TSH levels in Taltal.	OR for a family history of thyroid disease in all lifelong residents was 4.97 (95% CI, 1.29-19.17)

[a]Further details on the assessments of confounding are provided in the next section.

Table 30. Excluded Studies

Excluded studies	Reason for exclusion
Tèllez Tèllez *et al.*, 2005	45% of women from the exposed city delivered in the unexposed city.
Li *et al.*, 2000b	TSH measurements collected on first day after birth were excluded.
Amatai *et al.*, 2007	< 10% of newborns had thyroid hormones measured in first 36 hr after birth.
Cao *et al.*, 2010	Adjustments for urinary creatinine could have created false associations. No data in neonates.
Buffler *et al.*, 2006	Used the same data as Steinmaus *et al.* (2010), but did not focus on newborns.

Misclassification of thyroid hormone status: The studies discussed above assessed thyroid hormone status using a single measurement of thyroid hormone. Thyroid hormone levels can vary in individuals from day to day and within a day. This variability means that a single assessment of serum thyroid hormone concentration could lead to misclassification of true long-term thyroid hormone status in some individuals. Importantly though, any errors in misclassifying outcome are likely to be the same as those associated with misclassifying exposure: non-differential misclassification that will likely bias results to the null. As with exposure misclassification, if these errors could be corrected, the effects reported in the positive studies listed above would likely be even greater than those reported.

Confounding:

a. General concepts

Several general concepts were considered in evaluating confounding in these studies. The first is that a factor must be associated with both the exposure (perchlorate) and the outcome (thyroid hormones) of interest to cause confounding. A factor may be a strong determinant of thyroid hormone levels, but if it is not associated with perchlorate exposure then it is unlikely to cause important confounding (Axelson, 1978). For many of the factors potentially related to thyroid hormone levels such as menopause, premenarche, physical activity, c-reactive protein, thyroid antibodies, thyroid diseases, use of certain medications, and many others there is no evidence or plausible reason to support that they are also associated with perchlorate exposure. As such, there is no evidence or logical reason to believe that they are important confounders in the studies presented in this section.

The second general concept is that in order for a factor to cause important confounding, it not only needs to be associated with the exposure and the outcome of interest, but these associations must be fairly strong (Axelson, 1978). A factor that is only weakly associated with either the exposure or the outcome may still cause some confounding, but the impact of this confounding on the study result will usually be minor and likely unimportant.

An example of this is given below for thiocyanate. In this example, and in the other examples provided in this section, the focus is on those factors which would most likely cause confounding and bias, including those factors commonly referred to in the current perchlorate literature. Here, the potential effect of thiocyanate as a confounder on studies assessing T4 is assessed using the methods presented by Axelson (1978) (Table 31). In this example, the mean serum T4 concentrations for various levels of thiocyanate exposure were obtained using data from NHANES 2001-2. The thiocyanate categories used in this example are the tertiles of thiocyanate in women from NHANES 2001-2 (Steinmaus *et al.,* 2007). These categories were selected because they were the ones in which perchlorate-T4 associations were found to differ in Steinmaus *et al.* (2007). As shown in these analyses (Table 31), mean T4 decreases as thiocyanate increases from the lowest (< 750 µg/L) to the highest tertile (> 1800 µg/L), but this decrease is small. Because the effect of thiocyanate on T4 is small, even if the proportion of women with high thiocyanate levels is twice as high in a study's higher perchlorate-exposed group (e.g., 66.7 percent with high thiocyanate, last row) as in the study's lower perchlorate-exposed group (e.g., 33.3 percent with high thiocyanate, shaded row) this would have only a very small effect (1.4 percent) on the mean difference in T4 between the perchlorate higher and lower exposed groups. This example shows that even if thiocyanate exposure is associated with both thyroid hormone levels and with perchlorate exposure, these associations are likely too weak to cause the effects seen in Table 29. The same is likely true for many other factors such as race, age, sex, obesity, socioeconomic status, nitrate, and iodine. In other words, while it is possible that all of these factors could be associated with both thyroid hormone levels and perchlorate exposure, the magnitude of these associations are, like thiocyanate, probably too weak to cause important confounding. Thus, while they may cause some confounding (e.g., they could change an unadjusted odds ratio of 1.52 to an adjusted odds ratio of 1.53 as in Steinmaus *et al.,* 2010), the magnitude of the confounding effect will likely be too small to affect the overall study conclusions.

Table 31. Analysis of the Potential Magnitude of Confounding by Thiocyanate Using the Methods of Axelson, 1978

Thiocyanate (µg/L)	<750	750-1800	>1800	M_o	Mean Diff	Mean Diff
Mean T4 (µg/dL):	8.632	8.496	8.272	(µg/dL)	(µg/dL)	%
Lower perchlorate exposure	33.3%	33.3%	33.3%	8.47	Ref	Ref
Higher perchlorate exposure	31.7%	33.3%	35.0%	8.46	0.01	0.1%
	26.7%	33.3%	40.0%	8.44	0.02	0.3%
	21.7%	33.3%	45.0%	8.42	0.04	0.5%
	16.7%	33.3%	50.0%	8.41	0.06	0.7%
	0.0%	33.3%	66.7%	8.35	0.12	1.4%

M_o, mean T4 expected in a group of subjects with this distribution of thiocyanate; Mean Diff, mean difference in T4 in the lower perchlorate-exposed group minus the higher perchlorate-exposed groups; Ref, lower perchlorate-exposed reference group

A third general concept of confounding is that factors that are very rare are unlikely to cause significant confounding in large population-based studies. These factors include rare thyroid diseases, certain genetic conditions, and the use of certain medications known to impact thyroid hormone levels.

Fourth, it is important to note that each of the five positive studies listed in Table 29 involved different study populations, different time periods, different study methods, and different research groups. Despite all of these differences, the effects identified across all of these studies were similar and consistent. This consistency decreases the likelihood that confounding is responsible for all of the effects identified. It is possible that the same confounder affected each of these studies. However, some of these studies adjusted or stratified for several of the factors known to be among the most important population-wide determinants of thyroid hormone levels (age, sex, and race) and found these adjustments made very little difference. It is possible that those studies which did adjust or stratify for confounders were not impacted by confounding while those studies or analyses which were unadjusted were affected by confounding. However, there is no evidence or plausible reason to support that this is the case, and again, the consistency of the findings across the different studies argues against this. It is also possible that each of the five studies or analyses in Table 29 was affected by five entirely different confounders. However, it seems highly unlikely that five different confounders would all lead to essentially the same effect in five different studies and in five different study populations. All told, the consistency of the effects seen in the different studies in Table 29, combined with the fact that adjusted results showed essentially no evidence of confounding (see below), argues against the idea that confounding played a major role in these results.

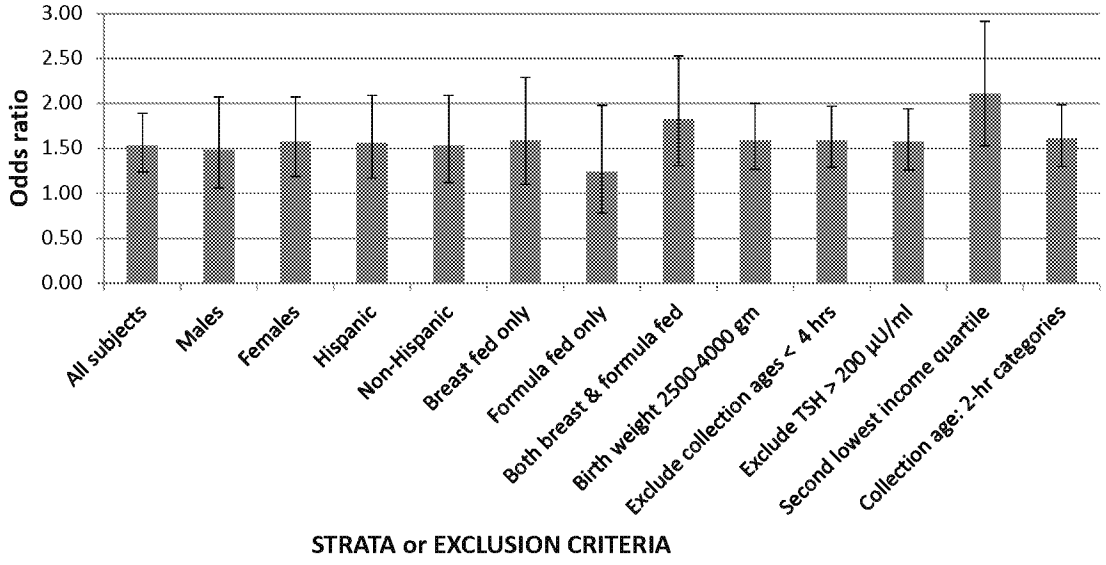
Finally, many of the factors related to thyroid hormone might not cause important confounding for the reasons given above, but they may still act either cumulatively or synergistically with perchlorate to decrease thyroid function. Certain factors such as nitrate and thiocyanate act by the same mechanism as perchlorate, and as discussed in the following sections, some evidence exists that people exposed to one or more of these agents may be particularly susceptible to perchlorate. For example, some perchlorate-thyroxine findings from NHANES suggest that thiocyanate, perchlorate, and low iodine intake could act cumulatively or synergistically (Blount *et al.,* 2006; Steinmaus *et al.* 2007; Steinmaus *et al.,* 2013). Other factors, such as polychlorinated biphenyls (PCBs) or anti-thyroid antibodies likely affect thyroid function by different mechanisms but might also act cumulatively or synergistically with perchlorate to adversely impact thyroid function. Importantly, this type of effect is not confounding, and is usually not evaluated or "controlled" in the same way as confounding. Instead, these types of effects would create groups of people who may be especially susceptible to perchlorate.

b. Evidence for or against confounding in each study

Steinmaus *et al.,* 2010: As discussed above, this study adjusted for many different potential confounding variables including age, gender, race/ethnicity, type of feeding, birth weight, and community average household income, and these had little impact on study results and no impact on study conclusions. For example, in the analysis of whether TSH levels were greater than 25 µU/mL in the first 24 hours after birth, the unadjusted odds ratio for having elevated TSH, comparing perchlorate-exposed and unexposed communities, was 1.52. After adjusting for age, gender, race/ethnicity, type of feeding, birth weight, and community average household income, the odds ratio was 1.53. Thus, the excess odds ratio changed by less than 2% with adjustment. This very small 2 percent change is strong evidence that none of these factors caused major confounding. It also provides evidence that residual confounding from incomplete adjustment of any of these factors is likely to cause effects that are even smaller than 2 percent.

In addition to statistical adjustments, the use of stratified analyses and exclusion criteria are two other ways of evaluating the role of confounding. Figure 8 shows the odds ratios for having a TSH level above 25 µU/mL comparing neonates from perchlorate-exposed and unexposed communities in analyses using a variety of stratification and exclusion criteria. As shown, statistically significant elevated odds ratios are seen in all analyses except the analysis of formula fed infants. The lower odds ratio in formula fed infants is consistent with the exposure misclassification soon after birth discussed on page 60 above. The fact that the elevated odds ratios remained in all the other analyses is evidence that none of these factors had important effects on results, or more importantly, on the conclusion that perchlorate exposure is associated with increased neonatal TSH levels in this dataset.

Figure 8. Odds Ratios for TSH > 25 µU/mL within 24 Hours of Birth Comparing Perchlorate-exposed (> 5 µg/L) and Unexposed (≤ 5 µg/L) Communities in Analyses Stratified by Age, Gender, Race/Ethnicity, Feeding Type, Birth Weight, or TSH Outliers (Steinmaus *et al.*, 2010) [The vertical lines are 95% confidence intervals]



Kelsh *et al.*, 2003: Using the data provided in the tables of this article, OEHHA estimated an odds ratio of 1.18 (95% CI, 1.13-1.24; $p < 0.0001$) for having a low T4 level and an odds ratio of 1.57 (95% CI, 1.14-2.16; $p < 0.0001$) for having an elevated TSH level. While it is possible these elevated odds ratios are due to some unknown confounding, several pieces of evidence argue against this. First, in the analyses done by Kelsh *et al.*, adjustments for birth weight, ethnicity, sex, birth year, age, and multiple births had little impact on the odds ratios they calculated. For example, comparing Redlands (exposed) to the rest of San Bernardino and Riverside Counties (unexposed), the odds ratio for having an elevated TSH level changed from 1.28 to 1.24 after adjustments for all of these factors. This small change suggests that none of these factors had important confounding effects in this study. Therefore, despite the fact that a few of these factors were shown to be related to neonatal TSH levels in this study (e.g., ethnicity and birth weight), they were not different enough between perchlorate-exposed and unexposed areas to cause major confounding. This provides strong evidence that the unadjusted odds ratios calculated by OEHHA are also not due to confounding by these factors since the OEHHA analyses involved the exact same perchlorate-exposed and unexposed areas used in the original authors' own calculations.

A second piece of evidence that the unadjusted odds ratio calculated by OEHHA is not due to confounding is the fact that this unadjusted odds ratio is remarkably close to the adjusted odds ratio in the corresponding analysis in Steinmaus *et al.* (2010). That is, for subjects with TSH collection ages within 18 to 24 hours after birth, the odds ratio for having TSH > 25 µU/mL was 1.57 using unadjusted data

from Kelsh *et al.* (2003) and 1.53 in the Steinmaus *et al.* (2010) adjusted analyses. The similarity of these two odds ratios, combined with the fact that adjustments or stratifications for age, gender, race/ethnicity, feeding type, birth weight, and community household income had little effect on the Steinmaus *et al.* (2010) results provides additional evidence that the elevated unadjusted odds ratio calculated by OEHHA using the Kelsh *et al.* (2003) data is not due to confounding by the factors adjusted for in Steinmaus *et al.* (2010).

Brechner *et al.*, 2000: An odds ratio of 1.18 (95% CI, 1.05-1.33; p=0.006) for decreased T4 and a 27 percent higher TSH level was found comparing perchlorate-exposed Yuma to unexposed Flagstaff. The T4 odds ratio was based on unadjusted data provided in the article while the TSH results were based on analyses stratified by age and race/ethnicity. In a subsequent Letter to the Editor, the authors state that the difference in TSH levels remained higher in Yuma than Flagstaff when sex, age, and race/ethnicity were included in the analysis of variance (p= 0.009), suggesting that these three variables were not strongly related to perchlorate exposure and were not responsible for the relationship between perchlorate exposure and TSH identified in this study. Because these three variables caused little confounding in the analysis by Brechner *et al.* (2000), and because the unadjusted odds ratio of 1.18 was calculated using the exact same perchlorate exposed and unexposed areas (Yuma and Flagstaff, respectively) as defined by the authors of this study, it is unlikely these factors confounded and are responsible for the elevated unadjusted odds ratio of 1.18 calculated by OEHHA. Lamm (2003) suggests that the differences in altitude between the two cities might be responsible for the effect identified. However, Lamm provides no evidence for this, and as discussed above, several studies show that altitude causes effects that are directly opposite to those proposed by Lamm (2003). The likelihood that other potential confounders such as socioeconomic status, iodine, or other environmental chemicals had major effects is discussed below.

Li *et al.*, 2000a: Based on data provided in Figure 3 of this article, newborn T4 levels on day 1 after birth appear to be about 22 percent lower in perchlorate-exposed Las Vegas than in unexposed Reno. On almost all other days after birth except day 1, T4 levels appear to be similar between the two cities. This pattern (effects seen on day 1 after birth but not later) is consistent with the likely impacts of exposure misclassification on maternal perchlorate-neonatal TSH relationships that occurs several days after birth (see pages 59-60). In the authors' analyses, adjustments for gender, birth weight, and age appear to have very little effect on results. For example, in the unadjusted analyses, the difference in mean T4 levels between Las Vegas and Reno was close to zero (mean difference = 0.01; means of 17.11 and 17.12 µg/dL, respectively; p = 0.901). In the adjusted analysis, this difference was also about zero (mean difference = 0.069 µg/dL, p = 0.407). As in the preceding studies, the very small difference between the adjusted and unadjusted analyses provides evidence that confounding had very little impact on these results and that age, birth weight, and

sex were not strongly enough related to both perchlorate exposure or thyroid hormone levels to cause substantial confounding.

Crump *et al.*, 2000: In an unadjusted analysis of TSH measurements collected on days 1-2 after birth, the median TSH level in the high exposure city of Taltal was 45% higher than that in the low exposure city of Antofagasta, although the sample sizes were small. Several factors suggest that this result is not due to confounding. First, TSH measurements were, in general, collected later in the exposed city of Taltal than they were in the unexposed city of Antofagasta. Since TSH levels tend to decrease with time after birth, based on this factor alone, one would expect that TSH levels would be lower in Taltal than Antofagasta. Given this, adjusting for age at the time of TSH collection would most likely increase, not decrease the difference seen between Taltal and Antofagasta. Second, in addition to the TSH findings, this study also reported elevated odds ratios (ORs) for a family history of thyroid disease in Taltal compared to Antofagasta (OR = 3.35, 95% CI, 1.19-9.38 in all subjects and OR = 4.97, 95% CI, 1.29-19.17 in lifelong residents). These odds ratios were adjusted for age, sex, and urinary iodine. The unadjusted odds ratio for a family history of thyroid disease in all subjects, which could be calculated using the data provided in their Table 3, was 2.85 (95% CI, 1.07-7.42). The fact that the unadjusted odds ratio is only a little lower than the adjusted odds ratio (2.85 versus 3.35) suggests that while age, sex, and urinary iodine had some confounding effects, the magnitude of this confounding was not strong enough to mask an association. The fact that age, sex, and urinary iodine did not cause significant confounding in the analysis of family history of thyroid disease provides that these factors are not likely to cause major confounding in the analysis of neonatal TSH levels. The notion that iodine is an unlikely confounder in this study is also supported by the fact that the mean urinary iodine levels reported in children in the two cities is very similar: 75.6 ± 40.4 µg/dL in Antofagasta and 76.6 ±47.4 µg/dL in Taltal. This similarity provides strong evidence that iodine was not related to this study's main metric of perchlorate exposure (city of residence) and thus was not likely a major confounder. Ethnic differences are unlikely to have caused the effects seen since there are no major ethnic differences between these cities. Finally, nitrate levels in these cities are below U.S. recommended levels, so nitrate was an unlikely cause of the positive effects seen.

c. Other data on confounding

In this section we evaluate the likelihood that various individual uncontrolled factors might have caused confounding in the studies discussed above. Since many different things can affect thyroid hormone levels, one could hypothesize that many different things could potentially cause confounding. However, since few are strongly related to perchlorate exposure, few are likely to cause confounding. Because of this, OEHHA chose not to evaluate each of the hundreds of different factors that can affect thyroid hormone levels, but rather chose those factors that seem to be discussed most often in the current literature on perchlorate. These factors include iodine, nitrate, other environmental

chemicals like polychlorinated biphenyls (PCBs), and thyroid antibodies. Other factors such as race/ethnicity and thiocyanate were discussed above. The age of neonatal sample collection is not discussed here since all of the studies in Table 29 either adjusted for or stratified by this variable.

Iodine and nitrate: Data from Blount *et al.* (2006) and Steinmaus *et al.* (2007) suggest that iodine is more likely to be an effect modifier than a confounding variable. In other words, findings from these studies suggest that low iodine intake (and high thiocyanate levels) are more likely to produce additive or synergistic effects on thyroid hormone levels with perchlorate than cause false associations between perchlorate and thyroid hormone levels. In both Blount *et al.* (2006) and Steinmaus *et al.* (2007), adjusting for thiocyanate and nitrate had little effect on the perchlorate-T4 regression coefficient in women with low iodine levels. While some studies suggest that nitrate intake may affect thyroid hormone levels, thyroid volume, or goiter, questions regarding actual intake levels, control for iodine intake, and blinding of outcome assessments raise concern about the validity of their results (Tajtakova *et al.,* 2006; Gatseva *et al.,* 2008). Also, common nitrate exposures in the U.S. may not be high enough to affect thyroid function. In a clinical trial, a nitrate dose of 15 mg/kg-day for 28 days did not decrease thyroidal iodide uptake or impact thyroid hormone levels in 10 healthy volunteers (Hunault *et al.,* 2007). This intake level is 5-20 times, or more, higher than average nitrate intakes reported in several populations in Europe and the U.S. (OEHHA, 2000). These findings suggest that nitrate is an unlikely cause of the effects identified in the positive studies discussed above. Although iodine intake has been shown to affect thyroid hormone levels, these effects may only occur at extreme values of iodine, not at the levels most commonly seen in the U.S. For example, Soldin *et al.* (2005) found little evidence of an association between urinary iodine concentrations and serum levels of T4 or TSH in NHANES. Since the potential for confounding is directly related to the strength with which the potential confounder is associated with the outcome of interest, these findings suggest that iodine is very unlikely to cause significant confounding unless studies are done in areas where a very large fraction of the population has very low iodine intakes (and this low intake is associated with perchlorate exposure).

Other environmental chemicals: Some studies have found associations between certain chemicals such as PCBs and thyroid hormone levels (Chevrier *et al.*, 2007), but these effects are generally small and there is little evidence that the relationship between PCB exposure and perchlorate exposure is strong enough that PCBs are likely to cause important confounding in studies of perchlorate and thyroid hormones. To further evaluate this, correlation coefficients between urinary perchlorate levels and serum PCB levels were calculated using data from NHANES 2001-2 (the same data used in Blount *et al.,* 2006 and Steinmaus *et al.,* 2007). As shown in Table 32 these correlations are very low and therefore too small to cause any significant impacts on the study results reported above.

Table 32. Spearman Correlation Coefficients (R) between Serum PCBs and Urinary Perchlorate, NHANES 2001-2

PCB	R	p-value	N
52	-0.04	0.09	1474
99*	0.04	0.09	2192
101	-0.01	0.64	2217
118	0.06	0.009	2217
153	0.05	0.01	2216
156	0.06	0.005	2206
180	0.05	0.01	2212
183*	0.01	0.38	2216
184	0.04	0.05	2217
194*	0.05	0.02	2191
199*	0.05	0.01	2202

*The congeners with correlation coefficients > 0.10 between the PCBs and neonatal TSH levels in Chevrier *et al.* (2007).

Thyroid autoantibodies: In its recent report on perchlorate, the American Thyroid Association (2006) calls thyroid autoantibodies "an important confounder in thyroid physiology." In order to evaluate the possibility that these might be important confounders, OEHHA used data from NHANES 2007-8 to evaluate the magnitude of the association between thyroid autoantibodies and serum T4 using linear regression analyses adjusted for age and sex. As shown in Table 33, the magnitudes of these relationships were very small suggesting that these antibodies are unlikely to be important confounders in general population-based studies.

Table 33. Age and Sex Adjusted Associations between Total Thyroxine (T4) (µg/dL) and Thyroid Autoantibodies in NHANES 2007-8.

	Coefficient	SE	p-value
Thyroid peroxidase antibody (IU/mL)	-0.000233	0.00121	0.85
Thyroglobulin antibody (IU/mL)	-0.000221	0.000208	0.31

Study size: Several of these studies involved a very large number of study subjects [Kelsh *et al.* (2003), Brechner *et al.* (2000), and Buffler *et al.* (2006)], and the p-values are less than 0.001. These very low p-values provide evidence that the elevated odds ratios identified in these studies are unlikely due to chance. In Brechner *et al.* (2000), although the odds ratio for low T4 was somewhat small (OR = 1.18; 95% CI, 1.05-1.33), the p-value was 0.006, which again, suggests that the excess odds are unlikely due to chance.

A lack of statistical power may have affected some of the smaller studies. If relative risks are expected to be fairly low (e.g., less than 2.0), large sample sizes are needed to detect statistically significant associations. The small sample sizes and relatively low prevalence rates of the outcomes of interest of some studies might have limited their ability to identify true effects.

Subject selection: There is a concern about the way the neonate blood samples were selected for TSH determination in the studies reported by Brechner *et al.* (2000), Kelsh *et al.* (2003), and Li *et al.* (2000b). In these studies, TSH levels were only measured in newborns who had low T4 levels. The TSH findings of these studies are still important, however, because they indicate that the risk of having *both* a low T4 level and a corresponding high TSH level is greater in newborns from perchlorate-exposed areas than in newborns from unexposed areas. This is important since people with both low T4 and high TSH are more likely to have real thyroid effects than people with just a high TSH level. For example, a high TSH reading in a person who does not have a correspondingly low T4 level could just reflect normal intra- or inter-individual variability, or laboratory or collection error. Regardless, in each of these studies, T4 was measured in all subjects and at least some evidence was seen in each study that perchlorate was associated with a decreased T4. Given the known relationship between T4 and TSH, these decreases in T4 levels are biologically consistent with the reciprocal increases in TSH that were reported. This consistency provides evidence that the associations identified between perchlorate and increased TSH are real effects and are not solely due to bias from selective TSH sampling.

Other susceptibility factors not accounted for: Another important issue in these studies is the overall lack of data on co-variates that might interact with perchlorate to impact thyroid function. None of these studies specifically investigated potentially susceptible subpopulations such as people who have low iodine intakes, smokers, people with anti-thyroid antibodies, or people with high intakes of nitrate or thiocyanate from foods. Risks of thyroid-related effects may be greater in these groups than in the general population samples that were used in the studies in Table 29.

The TSH surge: For the reasons discussed above, the first 24 hours after birth may be the most relevant period for assessing associations between maternal perchlorate exposure during pregnancy and newborn thyroid hormone levels. One potential complicating factor of measurements collected during this time is the normal physiologic surge in TSH that occurs soon after birth. The exact causes of this surge are unknown, but mechanisms related to cold exposure, the shock of birth, or an acute drop in maternal T4 have been proposed. As shown in Figure 9, TSH levels surge right after birth, typically peak at 30 minutes, then gradually fall to normal levels in the next 24-48 hours (Fisher and Klein, 1981). Several authors have warned against measuring TSH levels during this period because it can lead to an increased rate of false positives when screening for congenital hypothyroidism. In other words, many children who have TSH

readings above 25 µU/mL (the traditional cut-off point for this diagnosis) during the first 24 hours may have normal TSH readings a few days later and not require treatment for congenital hypothyroidism.

However, a clinical diagnosis of congenital hypothyroidism is not the only outcome that should be assessed when looking at the possible impacts of perchlorate. This diagnosis is generally associated with very large changes in thyroid hormone levels and severe effects if untreated. As discussed above, much more subtle changes in thyroid hormones have been associated with cognitive effects in children in several studies (Pop *et al.*, 1999, 2003; Haddow *et al.*, 1999; Klein *et al.*, 2001; Kooistra *et al.*, 2006; Vermiglio *et al.*, 2004). That is, small changes in thyroid hormone levels that are within normal reference ranges have been associated with significant decreases in IQ in children that were not clinically hypothyroid and showed no other evidence of thyroid problems. If researchers only focus on the more severe effect levels that are associated with most cases of congenital hypothyroidism, these more subtle effects will be missed. For this reason, researchers should not only evaluate whether perchlorate is associated with clinically treatable congenital hypothyroidism (and the large TSH changes associated with this diagnosis), but should also investigate whether perchlorate is associated with even smaller changes in thyroid hormone levels. In this regard, while the studies in Table 29 provide little evidence that perchlorate increases the rate of clinical congenital hypothyroidism, they do provide evidence that perchlorate is associated with more subtle changes in newborn thyroid hormone levels.

Health consequences are unknown: The long-term health consequences of the effects seen in Table 29 are unknown. As discussed below, subtle changes in maternal thyroid hormone levels during pregnancy have been linked to cognitive effects in the offspring. This suggests that the fetus is highly sensitive to any changes in thyroid hormone levels during pregnancy. It is unknown whether the neonate is similarly sensitive.

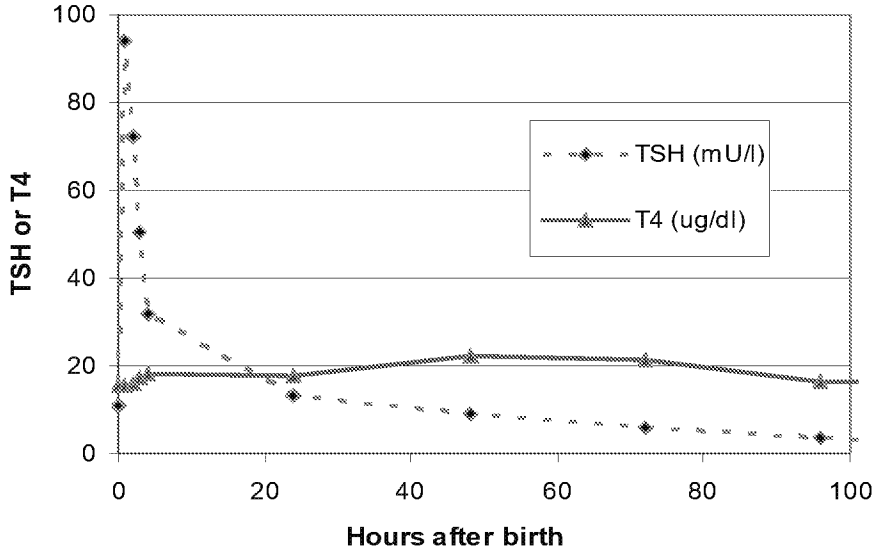
It is possible that the effects seen in Table 29 are also occurring in the fetus. This possibility is consistent with the well-established mechanism of perchlorate, by which a long-term continuous exposure would be expected to cause continuous effects on the thyroid. That is, if the mother is consuming drinking water contaminated with perchlorate during pregnancy, it would be expected that the fetus would be exposed to perchlorate during pregnancy and that some perchlorate would be present in the newborn immediately after birth. If this perchlorate exposure can lead to altered thyroid hormone levels in the newborn (as shown in Table 29), it seems likely that it is also doing so in the fetus. If perchlorate does impact thyroid hormone levels in the fetus, it may cause the same cognitive developmental impacts seen in the studies of maternal thyroid hormone changes during pregnancy (Pop *et al.*, 1999, 2003; Haddow *et al.*, 1999; Klein *et al.*, 2001; Kooistra *et al.*, 2006; Vermiglio *et al.*, 2004). Whether or not this is the case is currently unknown, and further research is needed to

determine if the effects seen in Table 29 are truly associated with long-term health outcomes.

It is possible that the effects reported in Table 29 are simply temporary effects that occur in the day-old newborn and do not occur in the fetus or older child. For example, it is possible that perchlorate somehow only affects the TSH surge, and either does not affect the thyroid at all (i.e., an extra-thyroidal mechanism), or does not affect the thyroid before or after the surge. There are several reasons to believe that this is not the case. First, the data in Table 29 are not consistent with an extra-thyroidal mechanism. If perchlorate were simply causing an increase in TSH by some extra-thyroidal process (that is, without first causing a low T4), then this increase in TSH would be expected to cause an *increase* in T4 levels. This was not seen. Instead, a perchlorate-associated *decrease* in T4 levels was seen in several studies. This suggests that the TSH effects are due to a perchlorate-associated inhibition of T4 production and a direct action on the thyroid gland. Second, TSH peaks about 30 minutes after birth (Figure 9), and the effects reported in Table 29 mostly involve measurements taken after the major part of this peak. For example, in Buffler *et al.* (2006), of all the newborns who had TSH levels measured in the first 24 hours after birth, less than one percent had measurements within the first three hours of birth. This small fraction suggests that any measurements collected during the highest points of the TSH peak had little impact on the Table 29 results. Finally, as discussed above, the hypothesis that the results seen in Table 29 simply represent a short-term temporary effect that occurs only in the day-old newborn (and not in the fetus) is inconsistent with the well-established mechanism in which a continuous dose of perchlorate is known to cause a continuous suppression of thyroidal iodide uptake and a continuous suppression of thyroid hormone production. Given the abundance of data supporting this mechanism, it seems somewhat implausible that some new and completely unknown mechanism, with no evidence to support it, would be causing these effects.

In summary, the data in Table 29 provide a consistent body of evidence linking perchlorate exposure during pregnancy with changes in thyroid hormone levels in the newborn. Currently, the long-term health implications of these effects are unknown. However, given the known mechanism of perchlorate, these effects may represent effects that are also occurring during the fetal period, which is a critical period of thyroid-hormone-dependent brain development.

Figure 9. Changes in Serum Neonatal T4 and TSH Levels by Hour after Birth (Abuid *et al.*, 1973; Cavallo *et al.*, 1980; Fisher and Odell 1969; Sack *et al.*, 1976) [Data are compiled by OEHHA from averaged individual thyroid hormone measurements from the cited studies from infants with blood collected at different times].



Studies of Perchlorate's Effects on Iodide Uptake and Thyroid Hormone

Clinical Dosing Studies

Stanbury and Wyngaarden, 1952. These investigators studied the effect of perchlorate on the discharge and uptake of iodide by the thyroid in Graves' disease patients. To study the effect of perchlorate on the discharge of accumulated iodide, they gave 30 mg of 1-methyl-2-mercaptoimidazole orally to eight patients. A dose of 200 mg of propylthiouracil was given to a ninth patient. One hour later, a tracer of ^{131}I was given. The accumulation of this isotope in the neck was recorded at frequent intervals until it leveled off. At this point, potassium perchlorate doses varying from 3 to 500 mg were given orally in small volumes of water. In each patient except the one treated with propylthiouracil there was a sharp fall in the counting rate within a few minutes after the ingestion. This always occurred within 30 minutes. With smaller doses the discharge of the ^{131}I was incomplete, but doses of 100 mg caused a fall in counting rates nearly equal to the counting rates recorded from the thigh (background). The investigators also reported that a single oral dose of 10 mg perchlorate caused about a 50 percent release of accumulated iodide. Potassium perchlorate doses as low as 3 mg (equivalent to 2.2 mg perchlorate) caused detectable, but incomplete, release of iodide from the thyroid. Assuming an adult body weight of 70 kg, this is equivalent to an oral dose of 31 μg/kg.

A LOAEL is not identified for this experiment because: (a) the number of patients per dose group is not known; (b) it is an acute exposure; (c) the patients suffered from a thyroid disease which might have affected iodide uptake; and (d) the patients were pretreated with drugs (either 1-methyl-2-mercaptoimidazole or propylthiouracil) that may enhance the release of iodide in the thyroid gland by preventing the oxidation of iodide ion to iodine and thyroid hormone synthesis.

To study the effect of perchlorate on the uptake of iodide in the unblocked gland, Stanbury and Wyngaarden (1952) gave 100 mg of potassium perchlorate to three patients and an hour later, tracers of ^{131}I. No thyroid hormone-disrupting drugs were given. Several days later each patient received a control tracer without previous perchlorate. In two cases, the studies were continued for 48 hours, but in the third, an observation period of only five hours was possible after the tracer. For the two patients with the long observation time, the control uptake was about 70 percent of the administered dose at 24 and 48 hours. When the patients were pretreated with potassium perchlorate, the uptakes were approximately 12 percent and 21 percent of the administered tracer dose at 24 and 48 hours following the administration of the tracer.

The duration of the inhibition of iodide uptake after the oral administration of 100 mg of potassium perchlorate (71.8 mg of perchlorate) appeared to be about six hours. Beyond six hours, accumulation of ^{131}I commenced. Durand (1938; as cited in Stanbury and Wyngaarden, 1952) found that at this time approximately half the administered dose of perchlorate has been excreted in the urine.

A LOAEL is not identified for this experiment because: (a) there were only two subjects that completed the experiment; (b) it is an acute exposure; and (c) the patients suffered from a thyroid disease which might have affected iodide uptake by the thyroid.

Godley and Stanbury, 1954. This study reported using potassium perchlorate to treat 24 patients with Graves' disease. Patients were treated with 600 to 1,200 mg/day for at least 11 weeks with a few as long as 52 weeks. Thirteen patients had determinations of the uptake of radioactive iodide by the thyroid both before beginning perchlorate therapy and within two weeks after medication had begun. The mean control uptake was 77.5 percent, with a range from 60.7 to 108 percent. The mean uptake during perchlorate therapy was 15.9 percent, with a range from 3.4 to 38.8 percent.

Bürgi *et al.*, 1974. This investigation studied the effects of perchlorate treatment on the release of endogenous iodide from the thyroid glands of five normal healthy volunteers (three females and two males). The volunteers were given ^{125}I-labeled iodide and ^{131}I-labeled T4 for seventeen days, followed by 3 x 200 mg/day (9.7 mg/kg-day) perchlorate for eight days. Analysis for the two tracers in the urine and serum of the subjects showed that this dose was sufficient to totally block iodide uptake by the thyroid. Additionally, the perchlorate treatment

caused an increase in excretion of non-thyroxine iodine of 65 percent above background.

Brabant *et al.*, 1992. In this study five healthy male volunteers were pretreated with 200 μg/day iodine for four weeks before perchlorate exposure. Iodine exposure was discontinued, and the volunteers were given 3 x 300 mg/day of perchlorate for another four weeks. Serum levels of T3 and T4 were measured at the end of the four-week perchlorate-dosing period. Perchlorate treatment had no effect on serum T3 or T4 levels or on thyroid gland volume. However, serum fT4 and TSH levels were significantly diminished by treatment, and thyroglobulin serum levels were almost doubled, indicating the stress of the treatment on the thyroid hormone balance. The perchlorate treatment also reduced intrathyroidal iodine levels.

In a follow-up study, Brabant *et al.* (1994, as cited in U.S. EPA, 2002) repeated the earlier studies with perchlorate treatment lasting longer than 4 weeks. As a result of the longer treatment, thyroid volumes increased in all subjects, although TSH levels did not increase.

Lawrence *et al.*, 2000. The investigators administered perchlorate to nine healthy male volunteers and monitored the impact on thyroid function. Each subject ingested 10 mg of perchlorate (as potassium perchlorate) dissolved in a liter of spring water for 14 days. Baseline serum TSH, total T4, total T3, 24-hour thyroid ^{123}I uptakes, serum and 24-hour urine perchlorate, and 24-hour urine iodine were determined. All blood and urine tests were repeated on days 7 and 14 of perchlorate administration, and 24-hour thyroid ^{123}I uptakes on day 14 of perchlorate administration. All tests were repeated 14 days after perchlorate exposure was discontinued. No effect of perchlorate was observed on serum T4, T3 and TSH (Table 34). It should be noted that the dietary iodine intake levels of the subjects were rather high, as indicated by the high urine iodine values (Table 35). Because iodide and perchlorate compete for the same receptor site on the sodium-iodide symporter (Wolff, 1998), a high dietary iodine intake may reduce the impact of perchlorate on the thyroid. There was no statistically significant difference in serum perchlorate levels after 7 days and 14 days of exposure, indicating no apparent accumulation of perchlorate in the systemic circulation over that period.

Table 34. The Effect of Perchlorate Administration (10 mg/day, about 0.14 mg/kg-day) for 7 and 14 Days on Thyroid Function Tests (Lawrence *et al.*, 2000)

Time	T4 (µg/dL)	T3 (ng/dL)	TSH (µU/mL)
Baseline	6.6 ± 0.4	136 ± 6	1.05 ± 0.14
Day 7 of perchlorate	6.7 ± 0.4	140 ± 8	1.00 ± 0.17
Day 14 of perchlorate	6.6 ± 0.5	151 ± 6	0.96 ± 0.12
14 days after perchlorate	6.5 ± 0.5	157 ± 9	1.23 ± 0.17

Values are mean ± standard error.

Table 35. Urine and Serum Perchlorate and Iodine Values before, during, and after Ingestion of 10 mg Perchlorate (about 0.14 mg/kg-day) for 14 Days (Lawrence *et al.*, 2000)

Time	Urine perchlorate (mg/24 hr)	Serum perchlorate (µg/mL)	Urine iodine (µg/24 hr)	Serum iodine (µg/dL)
Baseline	<0.5	0	254 ± 69	6.5 ± 0.42
Day 7 of perchlorate	7.7 ± 0.8	0.61 ± 0.02	233 ± 49	6.2 ± 0.34
Day 14 of perchlorate	7.5 ± 1.0	0.59 ± 0.02	385 ± 123	6.4 ± 0.37
14 days after perchlorate	<0.5	0	208 ± 42	6.3 ± 0.57

Values are mean ± standard error.

Lawrence *et al.* (2000) also reported that during perchlorate ingestion, there was a highly significant decrease in the thyroid ^{123}I uptakes at all three time points. In each instance, 150 µCi ^{123}I was administered to a subject and thyroid iodide uptake was measured at 4, 8, and 24 hours. The average decrease below baseline values over all three time points was 38 percent. Two weeks after perchlorate was discontinued, the 24-hour thyroid ^{123}I uptakes were significantly higher than baseline at 4, 8, and 24 hours (Table 36).

Table 36. Thyroid ^{123}I Uptakes before, during, and after Ingestion of 10 mg Perchlorate (about 0.14 mg/kg-day) Daily for 14 Days (Lawrence *et al.*, 2000)

Time	Thyroid ^{123}I uptake– baseline (% of dose)	Thyroid ^{123}I uptake 14 days on perchlorate (% of dose)	Thyroid ^{123}I uptake 14 days after perchlorate was discontinued (% of dose)
4 hours	12.5 ± 1.3	8.2 ± 0.7[a]	16.6 ± 2.4[b]
8 hours	17.3 ± 1.9	10.6 ± 1.0[a]	21.9 ± 2.8[b]
24 hours	23.6 ± 2.6	14.0 ± 1.6[a]	27.1 ± 3.3[c]

[a] $p < 0.01$ vs. baseline and after perchlorate treatment was discontinued
[b] $p < 0.01$ vs. baseline
[c] $p < 0.05$ vs. baseline
Values are mean ± standard error

Lawrence *et al.*, 2001. In a follow-up study, Lawrence *et al.* (2001) administered a daily oral dose of 3 mg of perchlorate to a group of eight healthy male volunteers for 14 days. They reported that the mean 8-hour thyroid radioactive iodide uptake decreased from 13.1 percent to 11.8 percent during perchlorate ingestion. Similarly, the 24-hour thyroid radioactive iodide uptake decreased from 16.1 percent to 14.5 percent, a 10 percent decrease that was not statistically significant. Assuming a default body weight of 70 kg, the dose used in this study is estimated to be 0.043 mg/kg-day.

Greer *et al.*, 2002. Daily oral doses of perchlorate (ClO_4^-) dissolved in 400 mL of water were given to groups of euthyroid human volunteers for 14 days. Subjects (4 male and 4 female; 18-57 years old) of each dose group were exposed to a daily dose of 0.02, 0.1, or 0.5 mg/kg of perchlorate (approximately 1.4, 7, or 35 mg, assuming 70 kg body weight). In a follow-up study, one additional subject of each sex received perchlorate at 0.02, 0.1, or 0.5 mg/kg-day, while six women and one man received a dose of 0.007 mg/kg-day. Subjects drank 100 mL of the perchlorate solution at 4 set times throughout each day. Measurement of 8- and 24-hour ^{123}I thyroid uptakes was performed prior to perchlorate exposure (baseline), on exposure days 2 and 14, and on post-exposure day 15. There was a strong correlation between the 8- and 24-hr uptakes over all dose groups and measurement days. There was no difference between exposure days 2 and 14 in the inhibition of uptake produced by a given perchlorate dose. There was no sex difference. Uptakes measured on post-exposure day 15 were not significantly different from baseline. Table 37 provides the 24-hour thyroid radioiodide uptake data by dose. The researchers measured total T4, fT4, total T3, and TSH in blood sampled throughout the study, and found them to be in the normal range for all subjects. One woman in the lowest dose group had abnormally high TSH on both the screening visit and on exposure day 14. Because of the limited data in the follow-up study, analysis of treatment effects on hormonal levels was confined to the 24 volunteers in the first study. Greer *et al.* (2002) reported no association between perchlorate dose and thyroid

hormone levels except a marginally statistically significant association with a decreased TSH in the 0.5 mg/kg-day dose group.

Table 37. Descriptive Statistics for the 24-Hour Thyroid Radioiodide Uptake Data from Greer *et al.*, 2002

Dose group	Time	Number of subjects in dose group	24-hr uptake (mean ± standard error)	
			Raw (%)	% of baseline
0.007 mg/kg-day	Baseline visit	7	18.1 ± 3.1	
0.007 mg/kg-day	Exposure day 14	7	16.5 ± 1.6	98.2 ± 8.3
0.02 mg/kg-day	Baseline visit	10	18.4 ± 1.2	
0.02 mg/kg-day	Exposure day 14	10	15.2 ± 1.1	83.6 ± 4.1
0.1 mg/kg-day	Baseline visit	10	19.9 ± 2.1	
0.1 mg/kg-day	Exposure day 14	10	11.0 ± 1.6	55.3 ± 3.9
0.5 mg/kg-day	Baseline visit	10	21.6 ± 2.0	
0.5 mg/kg-day	Exposure day 14	10	6.9 ± 0.9	32.9 ± 3.8

Braverman *et al.*, 2006. This investigation was a double blinded, randomized clinical dosing study in which 14 healthy volunteers received either placebo, or 0.5 mg, 1 mg, or 3 mg of potassium perchlorate once per day for six months. Nine of the subjects were women. Serum thyroid hormone and perchlorate levels, and urine perchlorate, iodine, and creatinine levels were measured monthly. Twenty-four hour radioactive iodide uptake (RAIU) was measured at baseline, and at 3 and 6 months of perchlorate ingestion, and one month after dosing was discontinued.

The mean urinary perchlorate level in the five subjects who received 0.5 mg/day was 332.7 µg (± 66.1) per 24 hours. The corresponding amount in the four subjects who received 3 mg/day of perchlorate was 2,079 µg (± 430) per 24 hours. Only one subject receiving the 1 mg dose completed the study and data on this subject was not reported. There were no significant changes in RAIU, T4, free T4 index (FTI), or TSH during or after the dosing period. The mean urinary iodine level in the 3 mg group was very high before the dosing started (322 µg/g creatinine; SD ± 357). This dropped to 192.8 µg/g (SD ± 110.1) one month after the dosing period. The large standard deviation suggests that this could be due to one outlying value, although the individual data on iodine were not shown.

The reason why this study did not find impacts on RAIU similar to other studies is unknown, although the authors note that this could be due to the small number of subjects, differences in dosing regimens (once daily versus semi-continuous), or the possibility that the NIS may be up-regulated as an adaptive response to long-term exposure. Given the fact that various metabolic and physiologic functions

have been shown to be less well developed and less effective in young children than in adults (Ginsberg *et al.,* 2002; Ginsberg *et al*., 2004), if chronic perchlorate exposure does cause the NIS to up-regulate, this might be less effective in young children than in adults.

Occupational Studies

Gibbs *et al*., 1998. This study monitored triiodothyronine resin uptake (T3U), total serum T4, FTI, and TSH levels in 18 workers occupationally exposed to ammonium perchlorate in air before and after a work shift. They also similarly monitored 83 workers who were not exposed. Based on the thyroid function test results collected, the authors concluded that exposure to a mean of 36 μg/kg-day ammonium perchlorate (ranging from 0.2 to 436 μg/kg-day) was not a significant predictor of the cross-shift change in any of the thyroid parameters. Given the relatively long serum half-life of T4 in adult humans (5-9 days) (U.S. EPA, 1998b), it would be very unlikely that serum T4 levels would exhibit a change over a single work shift.

Gibbs *et al*. (1998) also evaluated the thyroid function test results of workers exposed to ammonium perchlorate based on their working-lifetime dose estimates. They reviewed personnel records and employees were interviewed to determine the number of years worked in each of the seven exposure groups. An average of 2,000 hours worked yearly was assumed. Each subject's working-lifetime cumulative dose was then estimated as:

$$\sum [\text{mean group exposure}] \times [\text{years in exposure group}] \times 2{,}000$$

No significant correlations with estimated lifetime cumulative perchlorate dose were detected with any of the thyroid function measures (T3U, T4, FTI, and TSH levels). However, the tenure of the workers ranged from 1 to 27 years, while thyroid hormone levels are most likely to be affected by relatively recent perchlorate exposures (probably in the range of 1-3 months). Because of this, cumulative dose over a long period of time may not be the best metric for characterizing the effect of perchlorate exposure on thyroid hormone levels.

Lamm *et al*., 1999. This is a cross-sectional study of two similar worker populations from the same industrial complex: ammonium perchlorate production workers and sodium azide production workers. A total of 37 workers were exposed to airborne ammonium perchlorate, 35 males and two females. Twenty-one workers from the azide production plant served as the control group. Perchlorate exposure was measured using full-shift breathing zone personal air samplers for total as well as respirable perchlorate particles. Urinary perchlorate concentration was assessed at the beginning and end of the 12-hour shift in which the perchlorate exposure was measured. Post shift serum samples were collected for measurements of T4, T3, TSH, and anti-thyroid antibodies. The authors reported that there were no differences in thyroid function tests between workers in the azide and perchlorate plants or between the azide workers and

any of the three perchlorate-exposure groups (Table 38). Based on these data, a NOAEL of 0.48 mg/kg-day (33.6 mg/day divided by 70 kg) can be estimated. However, this data set has several limitations: (a) small sample size, (b) high dietary iodine intake among the workers, and (c) given the short biological half-life of perchlorate (approximately 8 hour), the exposed workers might recover from the effects of perchlorate during off-shift hours. Using the medical examination and questionnaire findings, Lamm *et al.* (1999) reported that worker exposures to perchlorate in the plant were not found to be associated with thyroid abnormalities.

Table 38. Perchlorate Exposures and Thyroid-Function Parameters, by Plant and Exposure Groups (Adapted from Lamm *et al.*, 1999)

Group	Total airborne perchlorate (mg/day)	Respirable airborne perchlorate (mg/day)	Absorbed dose (mg/shift)[a]	T4 (µg/dL)	T3 (ng/dL)	TSH (µU/mL)
Normal range				5 to 11	87 to 178	0.45 to 4.5
Azide worker	0.014±0.012 (n=4)	0.021±0.014 (n=6)	0.88±1.17 (n=21)	6.73±1.48 (n=21)	142.5±17.5 (n=21)	3.14±1.87 (n=21)
Perchlorate worker A	0.337±0.187 (n=6)	0.091±0.095 (n=11)	3.98±2.69 (n=14)	7.13±1.58 (n=13)	148.4±25.2 (n=13)	2.68±1.14 (n=12)
Perchlorate worker B	6.57±7.14 (n=2)	0.601±0.671 (n=7)	10.9±8.7 (n=8)	7.34±1.12 (n=8)	152.1±23.2 (n=8)	2.41±1.27 (n=8)
Perchlorate worker C	59.4±53.6 (n=12)	8.59±9.39 (n=14)	33.6±14.5 (n=14)	7.03±1.30 (n=15)	152.1±20.4 (n=15)	3.33±2.34 (n=15)

[a]Derived from urinary perchlorate concentration
Values are mean ± standard deviation

Braverman *et al.*, 2005. This was an investigation of RAIU and thyroid hormone levels in 29 workers employed in the same perchlorate production facility used in Lamm *et al.* (1999) and in 12 volunteers who did not work at the plant. All subjects were Caucasian males, and eight workers and two controls were smokers. The normal schedule for employees at the plant was to work three 12 hours shifts on three consecutive days and then have three days off work. Serum levels of perchlorate, thiocyanate, nitrite, T3, T4, FTI, and TSH and urine concentrations of perchlorate and iodine were measured just before (pre-shift) and just after (post-shift) the three day shift. Mean serum perchlorate levels in the workers increased from 2 µg/L to 838 µg/L from pre-shift to post-shift. RAIU decreased from 21.5 percent pre-shift to 13.5 percent post-shift (p-value for the difference < 0.01). The authors estimated perchlorate intakes based on differences in pre- and post-shift serum levels and used these estimates to plot dose-response relationships with RAIU. Figure 4 of their paper shows that perchlorate and RAIU relationship in this study was similar to that reported in Greer *et al.* (2002) and Lawrence *et al.* (2000, 2001). Interestingly, the RAIU

levels in the non-worker control subjects (14.4 percent) was significantly lower than the pre-shift level of the workers (21.5 percent, $p < 0.01$ compared to controls) and very similar to that of the post-shift level of the workers (13.5 percent, $p = 0.64$ compared to controls). The reason for this is unknown, although the authors note that this might be consistent with an apparent rebound increase in RAIU that has been noted in other studies. Post-shift workers had a slight but statistically significant increase in T3, T4, and FTI. The reason for this is unknown, although the authors hypothesize it may be due to a decreased iodine concentration in the thyroid enhancing the thyroid's response to TSH.

Although serum levels of thiocyanate and nitrate and urinary levels of iodine were measured, no data were presented on possible interactions between these variables and perchlorate on RAIU or thyroid hormone levels. The authors reported that exposure caused no statistically significant change in serum thiocyanate and nitrate levels but was associated with a statistically significant increase in urinary iodine:creatinine ratio. The pre-shift vs. just-after-shift means were 148 µg/g and 230 µg/g, respectively ($p = 0.02$). The mean urinary iodine:creatinine ratio in controls was 296 µg/g. The authors hypothesize that the increase in urinary iodine might have been a result of less dietary iodine being concentrated in the thyroid with perchlorate exposure.

Environmental Studies

Tèllez Tèllez *et al.*, 2005. Neonatal and maternal thyroid function were assessed in subjects from the following three cities (mean perchlorate levels in drinking water) in northern Chile: Taltal (100-120 µg/L), Chañaral (5-7 µg/L), and Antofagasta (non-detectable: <4 µg/L). The neonatal results are discussed in a preceding section. Serum fT4 and TSH measurements were collected from 184 women at two prenatal visits and one post-partum visit. No difference in mean fT4 or TSH was seen across the three cities at any of the three visits. For example, on the first prenatal visit (a mean of about 16 weeks gestation), the mean fT4 (in ng/dL) in the low, medium, and high perchlorate cities were 0.97 (SD ± 0.15), 0.95 (± 0.13), and 0.99 (± 0.13) (Kruskal-Wallis $p = 0.19$). Regression analyses showed no association between urinary perchlorate excretion and levels of fT4, TSH, and T3, although details of this analysis, such as whether urine concentrations were adjusted for urine dilution, or whether perchlorate concentrations were log transformed, were not reported. Maternal goiter was seen in all cities and increased from the first prenatal visit to the post-partum visit in both Taltal and Antofagasta, although the increase was greater in Taltal (from 9.4 percent to 22.5 percent) than in Antofagasta (from 8.7 percent to 11.1 percent).

As discussed in the section reviewing the neonatal findings of this study, maternal iodine levels were very high and it is possible that this may have protected the infants and the mothers from the impacts of perchlorate. Other factors that were also discussed above include: 1) similarity of the urinary perchlorate concentrations across the unexposed, low, and high exposure cities;

2) cesarean-section rates were markedly different across cities (cesarean section rates may impact chemical-thyroid hormone associations (Herbstman *et al.,* 2008)) ; 3) 45 percent of women from the exposed city gave birth in the unexposed city; and 4) there were few smokers (a common source of thiocyanate) and no data on thiocyanate levels. As discussed below, iodine, thiocyanate, and smoking may be important susceptibility factors in perchlorate-exposed women.

Gibbs and Van Landingham, 2008. This study involved a re-analysis of the data collected in the Tèllez Tèllez *et al.* (2005) study. In the previous paper, a regression analysis was done but very few results and details were provided. Most of the results presented in the previous paper were comparisons of mean thyroid hormone levels in each of the three cities. This may have diminished the ability of the study to identify a true effect since there was substantial overlap in urinary perchlorate concentrations across the cities. In this 2008 Letter to the Editor, Gibbs and Van Landingham used individual data on urine perchlorate, urine iodine, serum fT4 and TSH, and an interaction term for iodine and perchlorate in a linear regression analysis involving 150 women from the previous Tèllez Tèllez *et al.* (2005) study. Serum free T4 was entered into the model as fT4 unchanged or as $1/fT4^{½}$. The latter was used in order to achieve a normal distribution of the residuals, which is an assumption of the linear regression model. No associations were identified between urine perchlorate and fT4 or TSH (coefficients were only provided for statistically significant results). In addition, no associations were found in analyses restricted to subjects with urinary iodine levels below 100 µg/L, although this included only 16 subjects. Interestingly, in the analysis using the normalized fT4 variable (i.e., $1/fT4^{½}$), a statistically significant positive interaction was seen for iodide and perchlorate (regression coefficient (β) for the urinary iodide-perchlorate interaction = 6.26×10^{-7}; $p < 0.0001$). Given the apparent complexity of these analyses, and the lack of detail in this Letter to the Editor, the clinical meaning of this coefficient is difficult to interpret. The authors note that the coefficient for perchlorate itself was not significant in this analysis; however, the inclusion of an interaction term which includes perchlorate invalidates the use of the perchlorate regression coefficient for assessing any association with the dependent variable (Greenland, 1998). If these findings truly represent a perchlorate-iodide interaction, they would support the findings seen in Blount *et al.* (2006) described in the next section.

Blount *et al.*, 2006 and Steinmaus *et al.*, 2007. These are two studies which used data from the same cross-sectional investigation of urinary perchlorate levels and serum levels of thyroid hormones in 2,299 men and women ≥ age 12 years who took part in the 2001-2002 NHANES. NHANES is conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention (CDC) and is designed to assess the health and nutrition status of the non-institutionalized population of the U.S. This survey involves a complex multistage sampling design with some over-sampling in certain areas and among certain subgroups, but is designed to provide results that are nationally

representative. Information that is collected as part of this survey includes questionnaire data on demographic information, smoking, health history, and medication use. A single serum measurement of T4 and TSH and a single measurement of urinary perchlorate and iodine concentration were also collected. Other information collected included urinary creatinine, thiocyanate, and nitrate; and serum levels of albumin, cotinine, and c-reactive protein. Blount *et al.* (2006) assessed the relationship between serum thyroid hormone levels and urine perchlorate concentrations using a linear regression analysis adjusted for potential confounding variables and co-variates including age, urinary creatinine, estrogen use, c-reactive protein, cotinine, ethnicity, menopause, premenarche, pregnancy, fasting time, body mass index, and kilocalorie intake. Several factors including urinary perchlorate and creatinine and serum TSH were log-transformed to normalize their distributions. Exclusions included subjects with missing data on co-variates, a history of thyroid disease, current use of thyroid medications, extreme values of T4 or TSH (n = 3), and subjects missing perchlorate measurements. No association was found between T4 or TSH and perchlorate in men. In women, separate analyses were done for women with urinary iodine levels above and below 100 µg/L. This level was chosen since it is used by the World Health Organization to define iodine deficiency in a population. Thirty-seven percent of the women in this study had urinary iodine levels below 100 µg/L. The results of the analyses in women are shown in Table 39. A statistically significant association was seen between increasing TSH and increasing perchlorate in women with iodine levels above and below 100 µg/L. A statistically significant association was also seen between decreasing T4 and increasing perchlorate in women with urinary iodine levels below 100 µg/L, but not in women with iodine levels above 100 µg/L. The magnitude of this association ($\beta = -0.8917$) suggests that a ten-fold increase in urinary perchlorate (roughly the difference between the 10^{th} and 90^{th} percentiles) is associated with about an 11 percent decrease in T4. In pregnant women, this level of decrease is a little less than half of the decrease in T4 or fT4 associated with an average seven percent decrease in cognitive function in the offspring (see Table 20).

Table 39. Associations between Thyroid Hormone Levels and the Logarithm of Urinary Perchlorate in Women with High and Low Levels of Urinary Iodine (Blount *et al.*, 2006)

	Number of Subjects	Regression Coefficient (β)	Standard Error of β	p-value
Urine iodine < 100 µg/L				
T4	348	-0.8917	0.1811	<0.0001
Logarithm of TSH	356	0.1230	0.0373	0.0010
Urine iodine ≥ 100 µg/L				
T4	724	0.2203	0.3687	0.5503
Logarithm of TSH	697	0.1137	0.0506	0.0249

Differences in the numbers of subjects with an iodine category are due to differences in the number of subjects missing data on co-variates in each analysis. Except for perchlorate and creatinine, only co-variates with p-values < 0.10 were retained in each model.

Steinmaus *et al.*, 2007 used the same NHANES database and assessed whether other NIS inhibitors such as thiocyanate and nitrate might interact with perchlorate and iodine to affect thyroid hormone levels. Associations assessed by linear regression between thyroid hormones and urinary perchlorate were stratified by categories of nitrate, thiocyanate, smoking, and cotinine. Smoking and cotinine were evaluated since smoking is a major source of thiocyanate in many people and serum cotinine has been used in past studies as a biomarker for smoking intensity. The results of these analyses are shown in Table 40. In analyses of women with urinary iodine levels below 100 µg/L, regression coefficients between decreasing T4 and increasing urinary perchlorate were greater in smokers, those with high cotinine, and those with high thiocyanate levels than in non-smokers, those with low cotinine, and those with low thiocyanate, respectively. The magnitude of this association (β = -1.66) suggests that a ten-fold increase in urinary perchlorate (roughly the difference between the 10^{th} and 90^{th} percentiles) is associated with about a 20 percent decrease in T4. In pregnant women, this level of decrease is only a little lower than the decrease in T4 or fT4 associated with an average seven percent decrease in cognitive function in the offspring (see Table 20). These findings provide evidence that thiocyanate interacts with perchlorate and low iodine levels to decrease T4 production. The fact that similar effects are seen with all three methods used to categorize thiocyanate exposure (urine thiocyanate, serum cotinine, and smoking history) provides strong evidence that these findings are not due to chance. Interactions with TSH were seen in some analyses but not all and were not as clear as those seen for T4.

Table 40. Association between the Logarithm of Urinary Perchlorate (µg/L) and Serum T4 (µg/dL) and the Logarithm of TSH (µg/dL) in Women with Urinary Iodine < 100 µg/L, 2001-2002 NHANES (Steinmaus *et al.*, 2007)

	T4[a]				logTSH[b]			
	N	β	SE	p	N	β	SE	p
All	362	-0.73	0.22	0.004	369	0.13	0.05	0.02
Smoking[c]								
Current	63	-1.66	0.37	0.0005	62	0.13	0.11	0.23
Non-smoker	245	-0.54	0.23	0.04	245	0.11	0.03	0.009
Cotinine (serum)								
High (>10 ng/mL)	64	-1.47	0.30	0.0002	68	0.15	0.08	0.09
Medium[d]	185	-0.57	0.25	0.03	192	0.10	0.06	0.09
Low (ND)	101	-0.16	0.29	0.59	106	0.11	0.05	0.04
Thiocyanate (urine)[e]								
High (>1800 µg/L)	78	-1.67	0.40	0.0009	82	0.13	0.09	0.19
Medium	107	-0.68	0.37	0.09	108	0.20	0.04	0.0003
Low (<751 µg/L)	176	-0.49	0.30	0.11	178	0.10	0.05	0.06

Abbreviations: β, regression slope; ND, non-detectable; SE, standard error.
[a]T4 models were adjusted for fasting time, kcal, body mass index, c-reactive protein, nitrate, race, estrogen use, and pregnancy. T4 model with cotinine was also adjusted for menopause status.
[b]LogTSH models adjusted for age, fasting time, body mass index, race, premenarche, and lactation. LogTSH model with smoking status also adjusted for menopause status.
[c]Smoking data not available on all women and recent former smokers are excluded.
[d]Medium category includes all subjects with serum cotinine levels between 10 ng/mL and non-detectable.
[e]Thiocyanate categories based on tertiles in all women age 12 or older.

Analysis of Blount *et al.* (2006) and Steinmaus *et al.* (2007)

Blount *et al.* (2006) and Steinmaus *et al.* (2007) are key studies supporting two of the potential susceptibility groups identified by OEHHA (women with low iodine and women with high thiocyanate) and thus were evaluated in further detail. These studies have several strengths. First, they are based on individual rather than ecological data on perchlorate exposure and thyroid hormone levels. Second, information on a variety of potential confounders was collected and could be controlled for. Third, the studies involved a fairly large sample size, so the researchers could assess certain important susceptibility factors, like iodine status, sex, and thiocyanate intake that were not assessed in other studies. Some occupational and clinical studies, although they involved higher perchlorate exposure levels, may have missed the effects seen in Blount *et al.* (2006) and Steinmaus *et al.* (2007) because they did not specifically investigate susceptible groups. Fourth, the p-values for the associations identified were well below 0.05,

signifying that the probability these findings were due to chance is fairly low. Finally, the findings are biologically plausible in that they are consistent with the mechanism and direction by which perchlorate, iodine, and thiocyanate are all known to affect T4 and TSH levels.

There are also several potential concerns regarding these data. First, the studies are based on cross-sectional data and single measurements of urinary perchlorate, urinary iodine, and serum thyroid hormones. This could lead to some misclassification of true long-term exposure and thyroid hormone status. However, the half-life of perchlorate is short (about 8 hours in Greer *et al.,* 2002), and perchlorate seems to affect the thyroid fairly rapidly (less than one day in rats in Yu *et al.,* 2000). Because of this, shorter-term measures of perchlorate and thyroid status are probably better for assessing true associations than long-term measures. Also, since specimens were collected similarly in all subjects, any error resulting from not using the most relevant measure of perchlorate and thyroid hormone status would most likely cause a non-differential misclassification and likely bias towards the null, not towards the positive effects identified. The use of total T4 rather than free T4 (the physiologically available form) may also cause some misclassification, but again this would be expected to be non-differential and towards the null.

Urinary iodine levels for an individual can vary throughout the day and from day to day. Because of this fluctuation, it has been argued that measuring a single spot urinary iodine level is a poor reflection of an individual's overall, long-term iodine status. However, studies show that moderate to fairly strong correlations exist between single spot fasting urinary iodine concentrations and 24-hour urinary iodine concentrations, the recommended method for evaluating iodine deficiency in an individual (see Table 41). The fact that these correlations are not near zero suggests that while spot urinary iodine measurements may be associated with some misclassification, they still do provide at least some indication of true long-term iodine status in most people.

Table 41. Correlation Coefficients (R) of 24-Hour Urinary Iodine Levels with Single Spot Urinary Iodine Concentrations (µg/L) and Urine Iodine/Creatinine (I/Cr) Ratios

Author/Year	Location	N	R (for µg/L)	R (for I/Cr)
Konno *et al.*, 1993	Japan	22	0.83 ($p < 0.001$) (unknown)	0.699
Thomson *et al.*, 1997	New Zealand	333	0.49 ($p < 0.0001$) (log converted)	0.587
Knudsen *et al.*, 2000	Denmark	31	0.37[a] (Pearson)	0.61[a]
Rassmussen *et al.*, 1999	Denmark	21	0.61 ($p = 0.004$) (Spearman)	0.70

[a]Pearson correlation coefficient involves an assumption that the data are normally distributed; distortions of the true correlation can occur if they are not.

Urinary creatinine levels are commonly used to adjust urinary levels of other chemicals for urine dilution. Lamm *et al.* (2007) analyzed the NHANES 2001-2 data using the iodine:creatinine (I/Cr) ratio rather than iodine concentration and found no association between T4 and perchlorate in women with low I/Cr values. However, there are some concerns about the validity of using I/Cr ratios. The first is whether or not dividing a urinary analyte concentration by urine creatinine concentration actually increases the accuracy of classifying true long-term exposure to that analyte, either in an individual or in a group. Increasing evidence suggests that it does not (at least for some chemicals). As seen in Table 41, several studies show that correlations between I/Cr ratios and 24-hour iodine levels are no better than those seen with unadjusted urine iodine concentrations. Studies of other chemicals in urine have also shown that creatinine adjustment does not improve correlations with 24-hour urine levels or with biomarkers of effect (Hinwood *et al.*, 2002; Biggs *et al.*, 1997). One study presented in Table 41 did find an increased correlation coefficient after creatinine adjustment (Knudsen *et al.*, 2000). However, unlike the other studies in this table, this one presented Pearson correlation coefficients. These assume that variables are normally distributed (which many times urinary iodine levels are not) and can give highly distorted results if this assumption is not met.

As discussed above, the most likely bias from misclassifying true long-term iodine status would be bias towards finding no effect. The fact that the perchlorate-T4 association goes away in analyses stratified by I/Cr ratios suggests that the use of I/Cr leads to much more, not less, misclassification of true iodine status. One possible reason for this is that the concentration of creatinine in urine depends on many factors other than urine dilution. Dividing urine iodine concentration by urine creatinine concentration creates a variable with two components: iodine and creatinine. Between-person differences in I/Cr will depend on both the variability in iodine and the variability in creatinine. Thus, I/Cr is not only dependent on iodine excretion and iodine status, but is also dependent on creatinine excretion and all of its determinants. Studies have shown that while urine dilution may be a major determinant of urinary creatinine levels *within* an individual, factors such as age, sex, genetics, physical activity, muscle mass, and diet are major determinants of differences in creatinine excretion *between* individuals and may play an even greater role than urine dilution in determining inter-individual variation in urine creatinine levels (Barr *et al.*, 2005). People who have very high or very low levels of urine creatinine because of factors other than urine dilution will have their true iodine status misclassified if I/Cr ratios are used. Because urine creatinine concentration is dependent on all of these factors, using it to adjust for urine dilution may introduce a degree of misclassification of true iodine status which could overwhelm any improved accuracy that results from correcting for urine dilution. Based on these factors, several authors have concluded that I/Cr ratios should not be used for assessing iodine status (Bourdoux, 1993; Furnee *et al.*, 1994; Thomson *et al.*, 1996, 1997; Rasmussen *et al.*, 1999).

In summary, most evidence suggests that the findings in Blount *et al*. (2006) are not due to misclassification of exposure or outcome, and are not due to the cross-sectional nature of the study design. In fact, given that the most likely direction of the bias caused by these factors is towards finding no effect, if any misclassification of perchlorate, iodine, T4, and TSH could be corrected, the associations identified in these studies are likely to be even stronger than those reported.

Another potential problem with cross-sectional data is that one cannot be assured of the appropriate temporality; that is, that the exposure came before and caused the outcome, rather than the outcome coming before and causing the exposure. However, given the abundance of data showing that perchlorate can lead to a decrease in thyroid hormone levels, and no evidence for the opposite effect, it seems highly unlikely that the Blount *et al.* (2006) and Steinmaus *et al.* (2007) results represent an effect of thyroid hormones on urinary perchlorate levels.

Another potential concern in Blount *et al.* (2006) and Steinmaus *et al*. (2007) is the possibility of confounding. Although analyses included a number of potential confounding variables, some factors associated with thyroid hormone levels were not adjusted for. Importantly though, in order for a variable to cause confounding it must be associated with the exposure and the outcome of interest. If it is not associated with both, it cannot be a confounder. In addition, confounding should not be viewed as a qualitative issue, but rather as a quantitative problem. As stated in Rothman and Greenland (1998a), "It is the amount of confounding rather than the mere presence or absence that is important...." In order for a variable to cause important confounding, it must be strongly (not weakly) related to the exposure and outcome. If a variable is only moderately or weakly associated with the exposure and outcome it will likely cause little confounding and have only minimal impacts on results and overall conclusions (Axelson, 1978). It would be wrong to suggest that a variable that is unassociated with, or only weakly associated with, T4 or urinary perchlorate likely caused the relatively strong association between T4 and perchlorate identified by Blount *et al*. (2006).

In both the Blount *et al*. (2006) and Steinmaus *et al*. (2007) studies, the fully adjusted regression coefficients between T4 and perchlorate were very similar to the unadjusted coefficients. This suggests that although the potential confounders included in the models may have been related to the exposure, or to the outcome, or to both, none were related strongly enough to cause significant confounding. The impact of these variables at causing confounding can be assessed by looking at the effect of each one individually. Table 42 presents the results of the perchlorate-T4 linear regression analysis before and after each potential confounder is removed from either the unadjusted or fully adjusted model. As can be seen, removing any of the individual co-variates had less than a 20 percent effect on the magnitude of the perchlorate-T4 regression coefficient.

Table 42. Impact of Each Potential Confounding Variable on the Perchlorate-T4 Regression Coefficient (β) in Steinmaus *et al.* (2007)[a]

	Remove one variable at a time from the fully adjusted model			Add a single variable to the unadjusted model[b]		
	B	p-value	% change	B	p-value	% change
None	0.81	0.001	0%	0.78	0.002	0%
Creatinine	0.81	0.002	0%	0.63[b]	0.02	-19%
Age	0.85	0.0003	5%	0.80	0.002	3%
Fasting time	0.81	0.001	0%	0.79	0.001	1%
Albumin	0.83	0.001	2%	0.84	0.0006	8%
Kcals	0.80	0.0004	-1%	0.77	0.002	-1%
BMI	0.88	0.001	9%	0.71	0.004	-9%
C-reactive	0.83	0.001	2%	0.80	0.0008	3%
Nitrate	0.66	0.001	-19%	0.83	0.002	6%
Race	0.81	0.002	0%	0.78	0.0008	0%
Estrogen	0.78	0.002	-4%	0.77	0.002	-1%
Beta-blockers	0.84	0.001	4%	0.76	0.002	-3%
Menopause	0.79	0.0006	-2%	0.81	0.001	4%
Pregnant	0.80	0.0009	-1%	0.78	0.002	0%
Premenarche	0.80	0.001	-1%	0.74	0.003	-5%
Lactate	0.80	0.001	-1%	0.80	0.002	3%

BMI, body mass index

[a]All of the available potential confounders were entered into the model presented here. In Steinmaus *et al.* (2007) only those with p-values < 0.20 were added to and retained in the model. All analyses include the NHANES sample weights.

[b]The independent variables in the unadjusted model are the logarithm of perchlorate and the logarithm of creatinine. This is the coefficient with creatinine removed.

Some factors that might be related to thyroid hormone levels were not adjusted for in the NHANES studies (e.g., anti-thyroid hormone antibodies, PCBs, physical activity, menstruation disturbances). However, OEHHA is not aware of any evidence that these factors are associated strongly enough with perchlorate exposure that they would cause important confounding.

Nitrate has also been shown to be an NIS inhibitor. However, analyses of the NHANES 2001-2 urinary concentration data showed no evidence of an interaction of nitrate with perchlorate and iodine. The reasons for this are unknown, although some possible explanations are:

- Urine nitrate may not be an adequate reflection of serum nitrate or the concentration of nitrate reaching the thyroid gland and NIS.

- Variability in nitrate levels may be greater than variability in perchlorate and thiocyanate. Increased variability would decrease the statistical power of the study to find true associations.
- The *in vitro* studies in human cell lines which have assessed the relative potencies of iodine, perchlorate, thiocyanate, and nitrate may not be relevant to *in vivo* exposures.
- The nitrate exposures in NHANES may not have been high enough to affect thyroid function. In a clinical trial, a nitrate dose of 15 mg/kg-day for 28 days did not decrease thyroidal iodide uptake or impact thyroid hormone levels in 10 healthy volunteers (Hunault *et al.,* 2007). This intake level is 5-20 times or more higher than average nitrate intakes reported in several populations in Europe and the U.S. (OEHHA, 2000).

As a whole, although some of the details of the findings of Blount *et al.* (2006) and Steinmaus *et al.* (2007) remain unexplained, a thorough analysis of the major tenets of causal inference show that the overall results are generally consistent with known mechanisms and not likely due to chance, confounding, or other bias.

Pearce *et al.*, 2010. Urinary perchlorate and iodine concentrations and serum thyroid hormone levels were measured during the first trimester of pregnancy in 480 euthyroid women from Cardiff, Wales and 526 euthyroid women from Turin, Italy. Median urinary iodine levels were 117 µg/L in Cardiff and 50 µg/L in Turin. Median perchlorate levels were 2.6 µg/L (range, 0.3-49) in Cardiff and 5.2 µg/L (range, 0.2-168) in Turin. No correlation was found between urinary perchlorate concentrations and maternal T4 or TSH in either city. Analyses restricted to the large subset of women with urinary iodine levels below 100 µg/L gave similar results. Urine thiocyanate levels were low, much lower than those commonly found in the U.S. The median urine thiocyanate levels in Cardiff and Turin were 470.5 and 372.5 µg/L, respectively. In the NHANES study discussed above (Steinmaus *et al.,* 2007), the strongest perchlorate-thyroid hormone associations were found with thiocyanate levels in the upper tertile (i.e., above 1800 µg/L), and clear associations were not found with thiocyanate levels below 751 µg/L. In this regard, the Pearce *et al.* (2010) findings are consistent with those of Steinmaus *et al.* (2007).

Pearce *et al.*, 2012. In this cross-sectional study, urinary concentrations of perchlorate, iodine, and thiocyanate, and serum concentrations of TSH, free thyroxine (fT4), free triiodothyronine (fT3), and thyroperoxidase (TPO) antibodies were measured in 134 pregnant women from Athens, Greece, at a mean gestational age of 10.9 weeks (SD ± 2.3 weeks). Mean (± SD) concentrations were 6.5 µg/L (±11.2 µg/L) for perchlorate, 440 µg/L (± 318 µg/L) for thiocyanate, and 135 µg/L (± 77 µg/L) for iodine. In unadjusted analyses, a negative correlation was found between urine perchlorate and serum fT4 in all women (Spearman correlation coefficient (R) = -0.19; p=0.03) and in the subgroup of 50 women with iodine levels below 100 µg/L (R= - 0.23; p=0.09). However, in

multivariable regression modeling, with adjustments for urinary thiocyanate, urinary iodide, TPO titer, gestational age, and maternal age, a clear relationship between the logarithm of urinary perchlorate (µg/L) and the logarithm of serum fT4 (pmol/L) was not seen (regression coefficient (β) = -0.007; p=0.8). Gestational age was found to be inversely associated with fT4 in multivariable regression analyses (β =-0.003; p=0.002 for the association between gestational age in days and the logarithm of serum fT4), and positively correlated with urinary perchlorate concentration (R = 0.18; p=0.04). Based on these results, the authors hypothesized that gestational age appeared to be a confounder in the apparent correlation between urine perchlorate and serum fT4. The reason why gestational age was associated with urine perchlorate is unknown. In addition, unadjusted regression results were not presented, so regression analyses with and without adjustment for gestational age could not be compared. Mean thiocyanate concentrations were below those where the strongest associations between increasing urinary perchlorate and decreasing serum total thyroxine (TT4) were seen in NHANES (Steinmaus *et al.,* 2007). Associations between urinary perchlorate and TSH were not seen in correlation or regression analyses.

Leung *et al.*, 2012. Perchlorate, thiocyanate, and iodine in breast milk, and in maternal and breastfed infant urine (aged 1-3 months), and serum thyroid hormone concentrations in infants were measured in 64 infant-mother pairs from the Boston area. Median (range) perchlorate concentrations were 4.4 µg/L (0.5-29.5 µg/L) in breast milk, 3.1 µg/L (0.2-22.4 µg/L) in maternal urine, and 4.7 µg/L (0.3-25.3 µg/L) in infant urine. Urine iodine concentrations were 101.9 µg/L (27-570 µg/L) in mothers and 197.5 µg/L (40-785 µg/L) in infants. In multivariable regression analyses which included breast milk, maternal urine, and infant urine thiocyanate concentrations, no evidence of an association was seen between breast milk, maternal urine, and infant urine perchlorate concentration and infant serum fT4 (logarithm transformed) or TSH (logarithm transformed). For example, the regression coefficient between infant urinary perchlorate concentrations and the logarithm of infant serum fT4 concentrations was 0.004 (p=0.12) (units not provided). The authors noted that they were not able to achieve their targeted enrollment of 275 mother-infant pairs, and state that, "The recruited study population was underpowered to determine the statistical significance of perchlorate and thiocyanate exposures on serum infant thyroid function."

Mendez and Eftim, 2012 and Steinmaus *et al.*, 2013. Both of these studies used data from the 2007-8 NHANES to investigate associations between urinary perchlorate concentrations and serum concentrations of thyroid hormones. Compared to the original 2001-2 NHANES discussed above (Blount *et al.,* 2006; and Steinmaus *et al.,* 2007), serum thyroid hormone and urinary perchlorate concentrations were collected from a substantially larger number of subjects (5,921 versus 2,268) in NHANES 2007-8. In generalized additive mixed models, Mendez and Eftim (2012) reported associations between increasing creatinine-adjusted urinary perchlorate concentrations and decreasing serum TT4 and decreasing fT3 concentrations in the entire cohort and in separate analyses of males and females. For example, regression coefficients between perchlorate

(µg/L) and TT4 (µg/dL) in males and females were -0.0195 (p=0.01) and -0.0192 (p=0.03), respectively. Both perchlorate and TT4 levels were log-transformed. Similar associations were seen for fT4 in males but not in females. Additional co-variates in the models included age, ethnicity, tobacco smoking, medication use, body mass index, serum cotinine, and urinary iodine, thiocyanate, and phthalate ester metabolites. The authors stated that the models predicted reductions in serum TT4 of 0.46 µg/dL for males and 0.48 µg/dL for females (roughly a 6 percent reduction) for an increase in urinary perchlorate from the 5th to 95th percentiles. The Mendez and Eftim (2012) analyses were limited to only those 1,877 subjects who had data on urinary perchlorate, serum thyroid hormones, and urine phthalate ester metabolites. The authors noted that a previous study involving an overlapping subset of the NHANES subjects had identified a correlation between thyroid hormone levels and urinary phthalate ester and bisphenol A concentrations, "thus controlling for phthalate ester excretion was necessary to estimate the independent impact of perchlorate on hormone levels." Strong evidence of this type of confounding was not reported however.

In Steinmaus *et al.* (2013), subjects in NHANES 2007-8 were categorized into exposure groups based on their urinary perchlorate, iodine, and thiocyanate concentrations, and mean serum thyroxine concentrations were compared between groups. Analyses were adjusted for age, sex, and urine specific gravity. Subjects with urine perchlorate concentrations in the upper tertile (n=1,939) had TT4 concentrations that were 5 percent lower (mean difference=0.40 µg/dL, 95% CI, 0.14-0.65) than subjects in the lower tertile (n=2,084). Subjects with urine perchlorate in the upper tertile, urine thiocyanate in the upper tertile, and urine iodine concentrations below 100 µg/L combined (n=62) had TT4 concentrations 12.9 percent lower (mean difference=1.07µg/dL, 95% CI, 0.55-1.59) than subjects with lower perchlorate, lower thiocyanate, and adequate iodine concentrations (n=376). Similar findings were seen for fT4. Adjustments for other potential confounders including smoking, thyroid antibodies, fasting time, and medication use, or exclusions based on pregnancy, lactation, thyroid disease, or thyroid medication use had little impact on results. Overall, these results suggest that concomitant exposure to perchlorate, thiocyanate, and low iodine markedly reduces thyroxine production.

Bruce *et al.*, 2013. Bruce *et al.* (2013) used data from the same NHANES study as Blount *et al.* (2006) and Steinmaus *et al.* (2007), but the original serum samples were re-analyzed for serum TT4, TSH, fT4, thyroglobulin, thyroglobulin antibody, thyroperoxidase antibody, and several other factors. Measurements of fT4, thyroid antibodies, and some other factors were not available for the earlier analyses. In addition, the authors evaluated the role of perchlorate, thiocyanate, and nitrate in iodide uptake inhibition using perchlorate equivalent concentrations (PECs). The premise of this method is that the relative potencies of each agent on inhibiting iodide uptake in the thyroid can be multiplied by the concentrations of these agents in urine to determine their total combined impact on iodide uptake and thyroid hormone production. The authors reported that the overall PEC was weakly and negatively associated with serum TT4 levels. Using the

logarithm of total PEC and logarithm of TT4, the regression coefficient (β) was -0.0251 (p=0.020). However, similar associations were not seen for the logarithm of TSH (β = -0.0182; p=0.665) or free thyroxine (β = -0.0066; p=0.554). Other variables in the regression models included age, fasting time, body mass index, calories, ethnicity, serum albumin, use of certain medications, and other factors.

Importantly, the relative potencies used in this paper were based on the results of the Tonacchera *et al.* (2004) laboratory study. In this study, human sodium-iodide symporter (NIS) was transfected into Chinese hamster ovary cells, which were then seeded in 24-well plates and cultured in Dulbecco modified Eagle's medium containing 10% fetal calf serum. When the cells reached 100% confluence, the medium was removed, and the cells were washed with physiologic solution and combined with 500 mL buffer A (Hanks' balanced salt solution containing 0.5% bovine serum albumin and 10 mmol N-2-hydroxy-ethylpiperazine-N-2-ethanesulfonic acid) containing 100,000 counts per minute of carrier-free $Na^{125}I$. After the cells were incubated for 45 minutes at 37°C, they were washed twice with 2 ml of ice-cold buffer A, and solubilized with 1 ml of 0.1 mol/L sodium hydroxide. ^{125}I uptake was then determined by measuring the radioactivity counts per minute from each well. The doses causing a 50% decrease in iodide uptake for perchlorate, thiocyanate, and nitrate were 1.22 µmol/L (121 µg/L), 18.7 µmol/L (1086 µg/L), and 293 µmol/L (18,166 µg/L), respectively, and the relative potency of perchlorate (on a molar basis) was reported to be 15 and 240 times that of thiocyanate and nitrate. [For comparison, median serum levels of perchlorate, thiocyanate, and nitrate found in a recent study in pregnant women in New Jersey were 0.223 µg/L, 936 µg/L, 2410 µg/L, respectively (Blount *et al.,* 2009)]. It is not known how well human NIS in Chinese hamster cells simulates human NIS in human cells, how well hamster ovarian cells simulate human thyroid cells, or how well conditions in these wells simulate the complex environment of the human body.

Other unknowns regarding the Tonacchera *et al.* (2004) findings include: how the effects seen for the very high concentrations of perchlorate and the other agents used in this study correlate to effects that may be caused by lower, more common serum concentrations of these agents; how the thyroid and NIS auto-regulatory mechanisms in humans may affect relative potencies; how the fairly short-term exposures in this study correlate with the longer-term, more chronic exposures commonly seen with drinking water chemical exposures; whether or not there may be age-related or other susceptibility effects; how well the urine concentrations of each of the agents assessed correlate with the actual concentration of these agents at the NIS; what role the endogenous production of nitrate might play in affecting these relative potencies, the use of urine nitrate concentrations as an exposure metric, or auto-regulatory mechanisms; or how the presence of other agents or conditions that may inhibit the NIS, affect auto-regulatory mechanisms, or affect the thyroid in other ways might change the relative potencies reported in Tonacchera *et al.* (2004).

Gold *et al.*, 2013. In this study, serum thyroid hormone levels (fT4 and TSH) and questionnaire information on past and current doctor-diagnosed thyroid disease were collected from women who lived in an area with past perchlorate contamination. Subjects included approximately 300 women who resided near a National Priority List site in Sacramento, California, where five public drinking water wells contained between 93-250 µg/L of perchlorate. These high concentrations were thought to have begun in 1988 and ended in 1997 when the wells were capped. The study also included approximately 500 women from two neighboring comparison communities, one of which had significant airborne pollutant exposure and one of which had no noted high air or water contaminant exposure. The study did not begin, and serum thyroid hormone levels and questionnaire data were not collected, until > 4 years after the highly contaminated wells were capped. Overall, no association was found between past perchlorate exposure and thyroid hormone levels or past or current thyroid disease. The fact that thyroid hormone levels were not collected until several years after the high exposures were stopped limits the usefulness of this study since most evidence suggests that iodide uptake inhibition of perchlorate ends fairly rapidly (e.g., within a day) after the exposure is stopped (Greer *et al.,* 2002). In addition, questionnaire information on the presence of doctor-diagnosed thyroid disease is probably not a sensitive marker of the adverse effects of perchlorate exposure and its use would miss more subtle effects including the small thyroid hormone changes linked to cognitive effects in children discussed above (see pages 39-56).

Carcinogenicity

Morgan and Cassady, 2002. Morgan and Cassady (2002) assessed observed and expected numbers of new invasive cancer cases for all sites combined and 16 cancer types among residents of the greater Redlands area between 1988 and 1998. The community is known to have drinking water contaminated with perchlorate and trichloroethylene (0.09-97 ppb measured in 1980). They reported no significant differences between observed and expected numbers for all cancers, thyroid cancer, or 11 other cancer types. Significantly fewer cases were observed than expected for cancer of the lung and bronchus and the colon and rectum. More cases were observed for uterine cancer (standardized incidence ratio = 1.35; 99% CI, 1.06-1.70) and skin melanoma (standardized incidence ratio = 1.42; 99% CI, 1.13-1.77).

Li *et al.*, 2001. These authors compared the prevalence of thyroid cancer in Clark County (Las Vegas) which had measurable perchlorate concentrations in public water supplies to Washoe County, which did not. The relative risk was 0.75 (95% CI, 0.35-1.59).

Other Toxicities

Acute Toxicity

The acute lethal oral dose of perchlorate for an adult human was estimated to be 15 g, or 214 mg/kg for a 70-kg person (Von Burg, 1995).

Subchronic Toxicity

Potassium perchlorate has been used to treat Graves' disease in humans, and most of the early data on perchlorate in humans are in patients with this disease. Graves' disease is an autoimmune disorder in which patients carry immunoglobulins in their blood that bind to the TSH receptors on thyroid cells and act like TSH to stimulate DNA synthesis and cell divisions leading to a hyperthyroid state. Perchlorate inhibits the excessive synthesis and secretion of thyroid hormones by inhibiting the uptake of iodide into the thyroid and causes a discharge of accumulated iodide in the gland.

Godley and Stanbury (1954) report using potassium perchlorate to treat 24 patients with Graves' disease. Patients were treated with 600 to 1,200 mg/day for at least 11 weeks with a few patients treated for up to 52 weeks. Two patients developed gastrointestinal problems. In one patient, these effects occurred at 600 mg/day.

Crooks and Wayne (1960) administered potassium perchlorate at 600 to 1,000 mg/day to 200 patients with Graves' disease and observed one case of skin rash and three cases of nausea. In another group of 10 patients given 1,500 mg/day and 40 patients given 2,000 mg/day, five cases of skin rash, two cases of nausea, and one case of agranulocytosis occurred. Leukocyte counts returned to normal in the patient with the agranulocytosis when perchlorate treatment was stopped. The length of treatment was unclear but generally appears to have been less than 8 weeks.

Morgans and Trotter (1960) reported that three percent of 180 patients treated with 400 to 1,000 mg/day potassium perchlorate and 18 percent of 67 patients treated with 1,200 to 2,000 mg/day displayed a variety of adverse reactions that included skin rash, sore throat, gastrointestinal irritation, and lymphadenopathy. Based on the data reported by Crooks and Wayne (1960) and their own clinical observations, Morgans and Trotter (1960) recommended a daily dose of 800 mg/kg-day, a compromise between effectiveness and minimizing the toxic side effects of perchlorate.

Genetic Toxicity

No reports were found of studies that examined genetic endpoints (chromosomal aberrations, sister chromatid exchanges, etc.) in humans exposed to perchlorate.

Immunotoxicity

Weetman *et al.*, (1984) investigated the effect of perchlorate on human T and B cell responses to mitogen *in vitro.* Perchlorate at concentrations of 0, 0.01, 0.1, 1.0 and 10 mmol/L (1.17 g/L) were tested in cultures "designed to assess B and T cell responses." Supernatant immunoglobulins G and M (IgG and IgM) were measured by enzyme-linked immunoassays after culture of cells for 10 days with pokeweed mitogen. The investigators found that perchlorate at 0.1 to 10 mmol/L inhibited IgG production and at 10 mmol/L inhibited IgM production. They concluded that perchlorate has significant immunosuppressive activity at pharmacologically relevant concentrations that is not due to simple cytotoxicity (assessed by ethidium bromide/acridine orange fluorescence). However, the perchlorate concentrations in this study are in fact very high. A later study in Chinese hamster ovary cells expressing the human NIS (Ajjan *et al.*, 1998) showed perchlorate inhibition of iodide uptake evident at 0.01 micromolar, progressing to complete inhibition at 20 micromolar (0.02 mmol/L), which is much lower than the doses used in Weetman *et al.* (1984). Thus the immune effects of the high concentrations used in the study of Weetman *et al.* (1984) appear of doubtful relevance.

Hematological Effects

Graves' disease patients treated with perchlorate doses in the range of 6 to 14 mg/kg-day for three to eight months occasionally developed fatal aplastic anemia (Fawcett and Clarke, 1961; Hobson, 1961; Johnson and Moore, 1961). The mechanism of this blood disorder is not known. The use of perchlorate to treat Graves' disease was discontinued because of these cases. Nonfatal agranulocytosis was reported in patients treated with 14 mg/kg-day perchlorate for 12 days (Southwell and Randall, 1960) or three months (Sunar, 1963). Barzilai and Sheinfeld (1966) reported that 8 of 76 patients treated with 14 mg/kg-day perchlorate for at least two months developed leukopenia or other side effects. There was also one case of fatal aplastic anemia and one of fatal agranulocytosis within this group of 76 patients (Barzilai and Sheinfeld, 1966). As similar adverse hematological effects were not observed in rodents exposed to 30 mg/kg-day or 100 mg/kg-day, humans may be more sensitive than rodents for this endpoint.

5. TOXICOLOGICAL EFFECTS IN ANIMALS

The primary effect of perchlorate exposure is the disruption of thyroid hormone regulation. This mode of action is supported by the results of a number of animal studies that show that perchlorate inhibits thyroidal iodide uptake, changes serum T3, T4, and TSH levels, and subsequently causes a range of toxic effects. The animal studies, described in the section below, illustrate a range of effects that can result from the modulation of thyroid hormone regulation by perchlorate. As previously (OEHHA, 2004), human data described in earlier sections provide a reliable basis for the establishment of the PHG.

Adverse Effects on the Thyroid

Subchronic Studies of Effects of Perchlorate on the Thyroid

In many animal studies, perchlorate has been shown to perturb thyroid hormone regulation, induce hypertrophy and hyperplasia in thyroid follicular cells, and cause an increase in thyroid weight.

Shigan (1963) administered ammonium perchlorate to "white rats" at 650 mg/kg-day for one month and did not observe noticeable cumulative properties. The author also exposed "white rats" to ammonium perchlorate for three months at 190 mg/kg-day and found the treatment affected the regulation of the involuntary nervous system, caused changes in the protein fractions of the blood serum, and disrupted the liver's ability to produce glycogen for carbohydrate storage.

In a follow-up study, Shigan (1963) treated rabbits and "white rats" with 0, 0.25, 2.0, and 40 mg/kg-day of potassium perchlorate for 9 months. Many study details, such as the sex and number of animals in each dose group and the dosing medium, were not reported. In the two highest dose groups, the author found a significant increase in the amount of iodide excreted from the thyroid. It is not clear if the reported effect was seen in both species (U.S. EPA, 2002).

Caldwell *et al.* (1995) administered ammonium perchlorate to groups of Sprague-Dawley rats (six males and six females per group) in drinking water for 14 days at concentrations of 0, 1.25, 5.0, 12.5, 25, 50, 125 or 250 mg/L. The corresponding doses (male/female) in mg/kg-day are 0, 0.11/0.12, 0.44/0.47, 1.11/1.23, 2.26/3.06, 4.32/4.91, 11.44/11.47, and 22.16/24.86 mg/kg-day, respectively. At the end of the exposure period, thyroids were weighed, thyroid histopathology and morphometry examinations were performed, and thyroid hormone levels were measured with a radioimmune assay technique. The researchers reported that perchlorate exposure decreased circulating T3 and T4 and increased serum TSH. There is also evidence that rT3 (formed mostly in extrathyroidal tissues) and thyroglobulin levels were also increased. They also found that perchlorate exposure was associated with decreases in thyroid gland follicular lumen size and increases in relative thyroid weights. At the lowest

dose, 0.1 mg/kg-day, statistically significant changes in serum T4 were observed in both sexes; this level can be identified as a LOAEL.

Springborn Laboratories (1998) administered ammonium perchlorate via drinking water to male and female Sprague-Dawley rats (10 rats/sex/dose) at doses of 0, 0.01, 0.05, 0.2, 1.0, and 10 mg/kg-day for 14 and 90 days. An additional 10 rats/sex/dose were sacrificed after a 30-day recovery period following cessation of the 90-day exposure at doses of 0, 0.05, 1.0, and 10 mg/kg-day, to evaluate reversibility of any observed lesions. No statistically significant toxicological findings were observed among the groups with respect to clinical observations, body weights, food or water consumption, ophthalmology, hematology, or clinical chemistry. The researchers reported perchlorate exposure was associated with increased thyroid weights, thyroid follicular cell hypertrophy, and thyroid colloid depletion. Mean thyroid weights of male rats in the highest dose group were significantly increased after 14 and 90 days of exposure, while mean thyroid weights of female rats in the highest dose group were significantly increased after 90 days of exposure. No thyroid pathology was observed in other dose groups. After a 90-day exposure period followed by a 30-day recovery period, there was no increase in thyroid weight in either male or female rats in the 0.05, 1.0, and 10 mg/kg-day dose groups (Siglin *et al.*, 2000).

After 14 days of exposure, mean serum TSH levels were significantly increased in males at 0.2 mg/kg-day and higher, and in females at 0.05 mg/kg-day and higher, compared with the controls. Mean serum T4 levels were significantly decreased in both sexes at 10 mg/kg-day. Mean serum T3 levels were significantly decreased in males at levels of 0.01 mg/kg-day and higher. No statistically significant differences in T3 levels were observed in the female treatment groups.

After 90 days of treatment, mean TSH levels were significantly increased in males at 0.2 mg/kg-day and higher, and in females at 10 mg/kg-day only. Mean T3 and T4 levels were significantly decreased in both sexes at 0.01 mg/kg-day and higher. Based on this data set, a LOAEL of 0.01 mg/kg-day can be identified.

Following a 90-day exposure period and a 30-day recovery period, TSH levels were significantly increased in all three female recovery groups (0.05, 1.0, and 10 mg/kg-day), whereas no significant differences in TSH levels were observed in the male recovery groups. Mean T4 levels were significantly lowered in all three male recovery groups (0.05, 1.0, and 10 mg/kg-day), whereas no significant differences in T4 levels were observed in the female groups. Mean T3 level was significantly lower in females at 10 mg/kg-day. No statistically significant differences in T3 levels were observed in the male recovery groups (Siglin *et al.*, 2000). The authors did not speculate on the differences between the male and female data.

Siglin *et al.* (2000) noted there was a change in the mean TSH levels in the male and female control groups between 14 days and 120 days. They also found changes in mean T3 levels of control females over the course of the study. It was not clear if the observed variability in mean control hormone levels was reflective of normal age-related variations or due to other factors such as the relatively small sample sizes.

Studies of Perchlorate's Inhibitory Effects on Iodide Uptake by the Thyroid

The previous and subsequent section describes various studies that have documented the effects of perchlorate on thyroid and pituitary hormones as well as the thyroid of the treated animals. This section describes animal studies of perchlorate's effects on thyroidal iodide update.

Yu *et al.* (2000), working with the United States Air Force and U.S. EPA, investigated the inhibitory effects of perchlorate on thyroidal iodide uptake in rats. They injected perchlorate at 0, 0.01, 0.1, 1 or 3 mg/kg into groups of male Sprague-Dawley rats (six animals per dose and time point). At two hours post dosing, the rats were challenged with ^{125}I with carrier (33 μg/kg) by intravenous injection and euthanized at various time points post-dosing. Statistically significant thyroidal iodide uptake inhibition was found in the 1 and 3 mg/kg perchlorate dose groups at the 2, 6, and 9 hour time points. In addition, significant inhibition was also observed in the 0.1 mg/kg dose group at the 9 hour time point (Table 43).

Table 43. Percent Inhibition of Iodide Uptake in the Thyroid Gland of Male Rats (n=6) Dosed with Perchlorate (Yu *et al.*, 2000)

Time points	Perchlorate dose (mg/kg)	Mean iodide concentration in the thyroid (µg/g)	Thyroidal iodide uptake inhibition (%)[a]
2 hours	Control[b]	24.4	-
	0.01	21.3	13
	0.1	18.6	24
	1	7.4[c]	70
	3	3.0[c]	88
6 hours	Control[b]	46.5	-
	0.01	36.7	21
	0.1	32.0	31
	1	19.2[a]	59
	3	9.1[a]	80
9 hours	Control[b]	55.0	-
	0.01	49.2	11
	0.1[c]	39.2	29
	1	24.7[c]	55
	3	10.0[c]	82

[a]Percent inhibition = (control mean – dose mean) x 100 / (control mean)
[b]Dosed with ^{125}I with carrier only (33 µg/kg)
[c]$p<0.05$ compared to controls.

In a follow-up study, Yu *et al.* (2000) exposed groups of male Sprague-Dawley rats (6 animals per dose and exposure duration) to perchlorate in drinking water with target concentrations of 0, 1, 3, and 10 mg/kg-day continually for 1, 5, or 14 days. At the end of day 1, 5, or 14, rats were challenged once with 33 µg/kg ^{125}I with carrier and euthanized two hours later. Blood and thyroid gland were collected for analyses. A dose-related inhibition was noted in the one-day treatment group. The degree of inhibition was reduced over time and by exposure day 14, no inhibitory effect was observed in the 1 and 3 mg/kg-day groups. In a similar study, thyroid hormone profile of rats exposed to perchlorate was investigated. Male rats in groups of 8 were exposed to perchlorate in drinking water at 0, 0.1, 1, 3, and 10 mg/kg-day continually for 1, 5, or 14 days. In all treated groups, regardless of dose or exposure duration, TSH levels were increased compared to the control. The serum T4 levels were initially decreased in all dose groups except the lowest, 0.1 mg/kg-day. By 14 days, the 1 mg/kg-day dose group returned to control T4 values while T4 levels of the 3 and 10 mg/kg-day dose groups were still significantly depressed.

Yu *et al.* (2002) modeled the effects of perchlorate on the hypothalamus-pituitary-thyroid axis in the male rat. They found a high correlation between serum concentrations of perchlorate and percentage inhibition in thyroidal iodide uptake, irrespective of the route of administration. They found the hypothalamus-pituitary-thyroid axis responded quickly to perchlorate's blocking effects on thyroidal iodide uptake. Serum thyroid hormone levels decreased and serum TSH levels increased in response to perchlorate. Under the influence of TSH, the thyroid was up-regulated and was able to overcome the blocking effects of perchlorate by increasing its capacity to sequester iodide and produce hormones. Yu *et al.* (2002) noted that this is a dose-dependent phenomenon, which was overwhelmed by the blocking effects of high serum levels of perchlorate (corresponding to above approximately 1 mg/kg-day).

In Paulus *et al.* (2007), perchlorate-induced inhibition of thyroidal iodide uptake was measured in normally fed female Sprague-Dawley rats and in rats made iodine-deficient by long-term restriction of iodine in the diet (n = 10 rats per perchlorate-iodine group). In the iodine deficient animals, dietary iodine levels were 9-10 times lower than those in the normally fed animals. T4 levels in the iodine-deficient animals were 50 percent lower than in the normally fed animals, although TSH levels did not differ across the diet groups. Both groups were given a dose of ^{131}I via gavage, and ^{131}I uptake was measured in the thyroid. The proportion of administered ^{131}I taken up by the thyroid was greater in the iodine deficient rats than in the rats fed a normal diet.

Rats from each diet group were then given either no perchlorate or perchlorate at doses of 1.1, 5.6, or 28 mg/L, and percent of radioactive iodide uptake (%RAIU) was re-measured. In the normally fed rats, perchlorate produced significant inhibition of %RAIU at every dose group. In the iodine-deficient rats, %RAIU was decreased at all dose levels except the lowest dose of 1.1 mg/L (Figure 10), although the %RAIU reduction in the second highest dose group was not statistically significant. These results suggest that iodine-deficient animals are resistant to the iodide-uptake inhibiting effect of perchlorate compared to animals with adequate iodine intake. Based on this, the authors concluded that if the human NIS system reacts to iodine deficiency in a manner similar to the rodents in this study, iodine-deficient individuals may not represent a sensitive subpopulation for perchlorate toxicity. Importantly, this conclusion is based on a lack of findings in only one dose group. In addition, it is currently unknown whether these results apply to humans. Finally, the degree of iodine deficiency induced in the iodine deficient rats was fairly severe (the dietary iodine levels were one tenth of what they were in the normally fed animals). It is not known whether the effects seen in rats with this severe degree of iodine deficiency are relevant to the more moderate iodine deficiencies that are common in human populations.

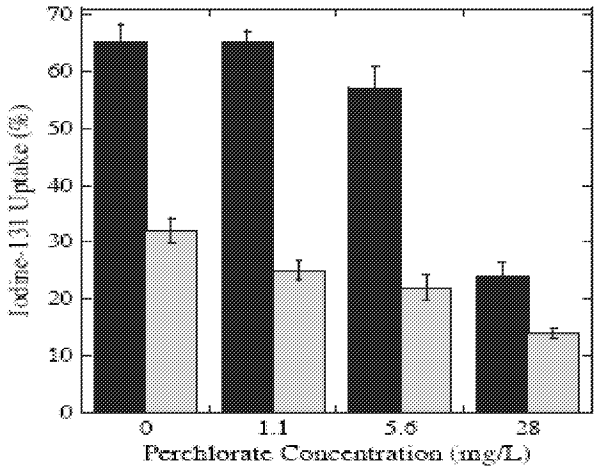


Figure 10. Dose-Response Relationship between Perchlorate and Radioactive Iodide Uptake in the Thyroid in Rats with Normal and Low Iodine Intake (Paulus *et al.*, 2007). Gray bars are values from rats fed a normal diet, black bars are values from rats fed a low-iodine diet. Values shown are mean ± SEM.

Clewell *et al.* (2001; 2003; 2007) have developed and attempted to validate rat and human physiologically-based pharmacokinetic (PBPK) models for the estimation of the effect of life stage and species on perchlorate and iodide inhibition kinetics. The models have been used to estimate perchlorate distribution in the male, pregnant, fetal, lactating and neonatal rat, and predict resulting inhibitory effects on thyroidal iodide uptake. The authors conclude that the fetal rat thyroid is most vulnerable to inhibition. Clewell *et al.* (2007) reported that "the fetus is predicted to receive the greatest dose (per kilogram body weight) due to several factors, including placental sodium-iodide symporter (NIS) activity and reduced maternal clearance of ClO_4^-."

Developmental and Reproductive Toxicity

A number of toxicity studies have shown that perchlorate exposure causes a variety of adverse health effects in the offspring of the test animals.

Developmental Toxicity

Postel (1957) gave a one percent solution of potassium perchlorate to eleven guinea pigs in the second or third week of pregnancy. The control group consisted of three sows receiving a diet containing 0.48 µg/g of iodine, distilled water *ad libitum*, and 50 mg of ascorbic acid orally twice a week. The treated sows were divided into four groups which received 0, 8, 16, or 32 µg, respectively, of triiodothyronine (T3) by subcutaneous injection each day. Control sows and those receiving potassium perchlorate alone were given daily injections of saline solution. The overall mean dose of potassium perchlorate

was 1,520 mg/kg-day in the T3-injected sows and 740 mg/kg-day in the group receiving only potassium perchlorate. The mean exposure duration was 37 days (range 21-48 days). One hour before the removal of the fetuses, radioactive sodium iodide was injected subcutaneously into the sow. Radioactivity of the blood and thyroids of the sows and fetuses were analyzed.

Postel reported that massive enlargement of the fetal thyroid was observed in all the perchlorate treated groups, with or without T3 injection. The overall mean weight was 491 mg/100 g body weight, compared with a mean control fetal thyroid weight of 32 mg/100 g body weight. Perchlorate did not cause enlargement of the maternal thyroid in any of the treatment groups, with or without T3 injection.

Postel (1957) also reported that the thyroid/serum radioiodide concentration ratio was approximately 175 in fetuses and 50 in sows in the control group. It was suggested that this finding supports the concept that the normal fetal thyroid is in a relatively hyperplastic state. The thyroid/serum radioiodide concentration ratios of both the perchlorate-treated sows and their fetuses were significantly lower than those of the controls.

Lampe *et al.* (1967) gave perchlorate-treated food to 12 rabbits from the beginning of pregnancy through gestation day 21 or 28. The rabbits were dosed at 100 mg/kg-day. No concurrent controls were used. Ingestion of perchlorate was found to cause an increase in maternal and fetal thyroid weights. On the 21st day of treatment, the maternal thyroid weights in treated animals were nearly three times higher than control thyroids; fetal thyroids from the treated animals were nearly four times the control weights. Continued intake of perchlorate further enhanced the increase in thyroid weight, particularly in the fetus. On the 28th day of treatment, the maternal thyroid weights in treated animals were nearly four times higher than control thyroid weights, and fetal thyroid weights from treated animals were nearly nine times higher than control thyroid weights.

Sztanyik and Turai (1988) investigated the safety of using potassium perchlorate or potassium iodide as blocking agents to prevent the uptake of radioiodine by fetuses. They injected these compounds into pregnant albino rats (body weight 200 to 250 grams) in amounts sufficient to "significantly decrease" uptake of radioiodine by the fetuses (0.1 to 6.0 mg potassium perchlorate per adult rat). There was no evidence of embryo- or fetotoxicity at these doses. In summary, the results of this study, and those of Postel (1957) and Lampe *et al.* (1967), all provide evidence that perchlorate can pass through the placenta from the mother to the fetus and affect the fetal thyroid in test animals.

A developmental neurotoxicity study of ammonium perchlorate in rats was conducted by Argus Research Laboratories (1998a; 1998b; 1998c). Ammonium perchlorate was administered to groups of 25 female Sprague-Dawley rats via drinking water at target doses of 0, 0.1, 1.0, 3.0, and 10 mg/kg-day. The dosing period was from the beginning of gestation (GD 0) to postnatal day (PND) 22.

Five dams per group were selected for sacrifice and blood collection on PND 10. Pups (F1 generation) were counted and clinical signs recorded daily during pre- and post-weaning. Some of the pups were assigned to four different subsets for additional evaluations: Subset 1 for brain weight and neurohistological examination on PND 12; Subset 2 for passive avoidance testing, water maze testing, and blood collection for thyroid and pituitary hormone analysis; Subset 3 for motor activity evaluation and auditory startle habituation; Subset 4 for regional brain weight evaluation and neurohistological examination on PNDs 82 to 85. U.S. EPA (2002) analyzed the F1 data and concluded that perchlorate treatment was associated with: (a) brain morphometric changes in the 10 mg/kg-day dose group and possibly also the 3 mg/kg-day dose group; (b) thyroid colloid depletion, hypertrophy, and hyperplasia in the 0.1 and 3 mg/kg-day dose groups; (c) thyroid hormone (T3 and T4) changes in the 0.1 and 1 mg/kg-day dose groups; and (d) increases in motor activity in some dosed animals.

Argus Research Laboratories (1999; York *et al.*, 2001) reported a two-generation reproductive toxicity study in Sprague-Dawley rats. Male and female rats (30 rats/sex/group) of the first generation (P) were exposed to ammonium perchlorate in drinking water at 0, 0.3, 3, and 30 mg/kg-day. One male and one female were allowed a cohabitation period of a maximum of 14 days. Lactation day (LD)1, postpartum, was defined as the day of birth. Rats that did not deliver a litter were sacrificed on gestation day 25 and examined for pregnancy status. At the end of the 21-day postpartum period, all surviving P rats were sacrificed. Pups not selected for continued evaluation were also sacrificed on LD 21. The selected F1 pups were dosed during the post weaning, cohabitation, and lactation periods. All F1 generation dams and their litters (F2 generation) were sacrificed on LD 21. York *et al.* (2001) reported that perchlorate is not a reproductive toxicant in the doses tested. In both the P and F1 adult rats, there were no deaths, abortions, or premature deliveries. No changes were reported in any sperm parameters in either P or F1 adult male rats nor on mating or fertility parameters in either P or F1 adult female rats (estrous cyclicity, fertility index, number of days in cohabitation, and number of rats mated). Natural delivery and litter observations for both F1 and F2 generation pups were comparable among the treated and control groups. Treatment-related effects were not observed on the gestation index, the number of dams delivering litters, the duration of gestation, the average number of implantations, the average number of live pups, the viability and lactation indices, the sex ratios, or the pup body weights.

York *et al.* (2001) found that perchlorate exposure caused statistically significant, dose-dependent changes in thyroid weight, histopathology, and hormone levels in P, F1, and F2 generation rats. Relative thyroid weights were significantly increased in the 30 mg/kg-day dose group for both sexes in the P generation and for F2 generation pups. However, in the F1 generation adult rats, relative thyroid weights were significantly increased in all dose groups for females and in the 3 and 30 mg/kg-day dose groups for male rats. All three generations developed hypertrophy and hyperplasia of thyroid follicular epithelium that increased in incidence and severity in a dose-related manner. Dose-related changes in TSH,

T3, and T4 were also observed in the treated rats. However, these changes were inconsistent among the different generations, sexes, and ages of animals.

U.S. EPA (2002) noted that two male rats from the high dose group (30 mg/kg-day) in the F1 generation (second parental generation) in the study had adenomas of the thyroid. These males were dosed from conception to 19 weeks of age. Without incorporating historical data, the difference between 0/30 in the control and 2/30 in the 30 mg/kg-day is not statistically significant by standard tests (e.g., Fisher's exact). However, using two earlier reported background incidence rates of 3.6 percent and 3.9 percent for thyroid follicular cell adenomas in male Sprague-Dawley rats in 2-year studies and Bayesian analysis, U.S. EPA (2002) determined the increase in thyroid follicular cell adenoma at 19 weeks in male Sprague-Dawley rats exposed to 30 mg/kg-day to be statistically significant.

Effects of perchlorate on motor activity in Sprague-Dawley rats were studied by Bekkedal *et al*. (2000). The females were dosed with ammonium perchlorate in drinking water for two weeks at 0, 0.1, 1, 3, or 10 mg/kg-day prior to mating with the breeder males and through PND 10. As dosing was stopped on PND 10, it is likely that the pups were not directly exposed to perchlorate in drinking water. On PND 14, one male and one female were randomly selected from each litter to be used in the motor activity testing. These same animals were tested on PND 14, PND 18, and PND 22. Pups were individually tested in automated Opto-Varimex Activity boxes where 9 different measures of activity were recorded for 90 minutes on each test day. Data were analyzed in 9, 10-minute blocks using a repeated measures ANOVA.

Bekkedal *et al*. (2000) reported no statistically significant differences for any of the nine measures of motor activity, and there were no reliable interactions related to treatment. A general pattern in the results was noticed. The authors suggested that there was a divergence in activity between the control and treated groups which emerged late in the 90-minute testing sessions.

U.S. EPA and NIEHS used a Bayesian hierarchical model to analyze the motor activity data reported by Argus Research Laboratories (1998a) and Bekkedal *et al*. (2000). They built a linear mixed-effects regression model relating dose, sex, age, habituation time and a habituation time × dose interaction term to the expected number of ambulatory movements, with an animal-specific intercept included to account for within-animal dependency (U.S. EPA, 2002). U.S. EPA concluded that there was evidence of an increasing dose-response trend in motor activity in both data sets, and suggested that the lower limit on the estimated dose corresponding to a 10 percent increase in motor activity relative to control can be used as a surrogate for the NOAEL. Because of the variability in the Argus Research Laboratories (1998a) study, a NOAEL that relied on the Bekkedal *et al*. (2000) study was chosen at 1 mg/kg-day to represent effects on motor activity from these combined data.

Argus Research Laboratories (2001) studied the effects of perchlorate on thyroid and brain development both during gestation and postnatally. Perchlorate was administered in drinking water to female rats two weeks prior to cohabitation at 0, 0.01, 0.1, 1, or 30 mg/kg-day and continued through the day of sacrifice. F1 generation rats were not directly dosed but might have been exposed *in utero* during gestation and via maternal milk and maternal water during the postpartum period. The rats were selected only from female rats that had litters of at least 12 live offspring at the time of cesarean-sectioning (Part A) or at the time of the first tissue collection (Parts B and C). P generation rats assigned to Parts B and C that delivered a litter were sacrificed on either PND 9 (Part B) or PND 21 (Part C). The thyroid and brain from one male and one female pup per litter were selected for histological and morphometric evaluation, with one set evaluated on PND 4, PND 9, and PND 21. Details of the study and findings are described in the study report prepared by the Argus Research Laboratories (2001), and a summary of the findings and evaluations is provided below.

According to the report, there were no deaths, adverse clinical observations or necropsy findings during the premating, gestational and/or lactation periods that were treatment-related in Parts A, B, and C. There were 16 pregnant dams in Part A. No treatment-related changes were found in cesarean-sectioning or litter parameters. There were 15 or 16 pregnant dams for Parts B and C that delivered. Natural delivery was unaffected by the treatment and all clinical and necropsy observations in the F1 generation pups were considered unrelated to the treatment.

The absolute and relative thyroid weights of dams at the highest dose were increased. The absolute thyroid weights of some pups exposed at 1 and 30 mg/kg-day were increased. Furthermore, the absolute thyroid weights of the PND 9 male pups in the 0.01, 0.1, 1 and 30 mg/kg-day dose groups were significantly increased over the controls.

An exposure-related increase in the incidence and severity of decreased colloid was noted in dams in the 1 or 30 mg/kg-day groups. Similar observations were made on the fetuses at birth and pups at PND 4 and PND 9. An increased incidence of follicular cell hypertrophy and/or hyperplasia was found in dams in the 30 mg/kg-day dose group. An increased incidence of follicular cell hyperplasia was also found in the 1 mg/kg-day dams sacrificed on PND 21.

In Part A, maternal TSH levels were significantly increased and T4 levels were significantly decreased at all exposure levels. Fetal TSH levels were significantly increased at 1 and 30 mg/kg-day while T3 was significantly decreased at all exposure levels. Changes of both the maternal and fetal thyroid hormone levels occurred in an exposure-dependent manner.

Maternal and fetal thyroid and pituitary hormone levels were also affected by various doses of perchlorate in Parts B and C. Most changes occurred in an exposure-dependent manner. In the PND 21 male pups, TSH levels were

significantly increased and T4 levels were significantly decreased at all exposure levels. T3 levels were also significantly decreased in the 1 and 30 mg/kg-day groups. In the PND 21 female pups, TSH levels were increased at all exposure levels, reaching statistical significance in the 0.1, 1, and 30 mg/kg-day groups. T4 levels were decreased with increased exposure but did not reach statistical significance.

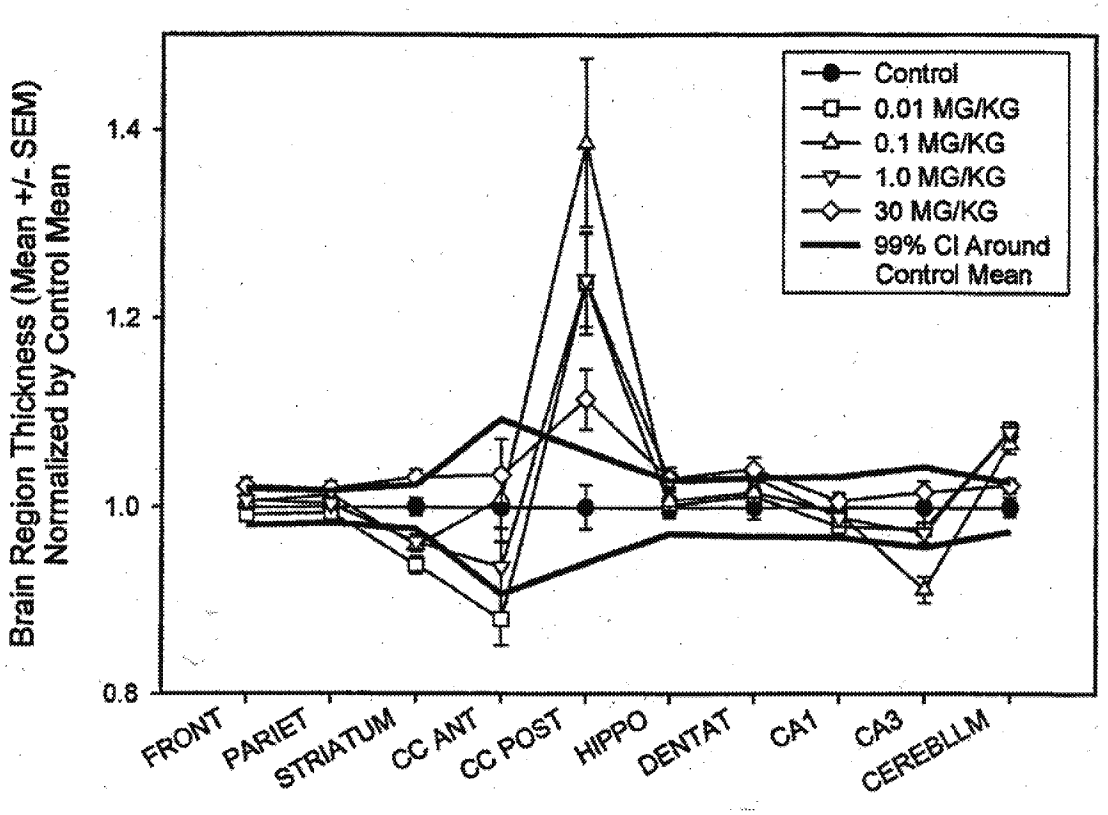


Figure 11. Profile Analysis of Brain Morphometry Measurements for PND 21 Rat Pup Brain Regions. The male and female linear thickness measurements were combined and normalized by the control mean of each region. The control data are represented by the horizontal line at 1.0. Profile analysis determines whether the vectors of measurements from each treatment group differ from each other and control in a dose-dependent fashion. The heavy line represents the ±99 percent confidence interval around the mean control values. Note that while this plot uses the normalized data to more easily illustrate the data vectors, the actual analysis was performed using raw data values (from U.S. EPA, 2002).

Size of various brain areas was also measured in brain sections from the PND 9 and PND 21 pups. Due to signs of disruption or damage found in the PND 9 sections that might have compromised the measurements, U.S. EPA (2002) relied upon the PND 21 measurements. In the PND 21 brains, the striatum, cerebellum, and corpus callosum in the exposed animals all showed significant differences from those of controls with the lowest administered dose of ammonium perchlorate, 0.01 mg/kg-day. As shown in Figure 11, different brain

regions show an inverted U or U-shape dose response. For instance, the corpus callosum showed a notable increase in linear extent of 24 percent or more at PND 21 in the 0.01, 0.1, and 1 mg/kg-day dose groups; however, this effect was not observed at the highest dose group, 30 mg/kg-day. Using these data, U.S. EPA (2002) identified a LOAEL of 0.01 mg/kg-day for the adverse effects of ammonium perchlorate on the developing brain in rats. This is equivalent to 0.0085 mg/kg-day for the perchlorate anion alone.

Thuett *et al.* (2002) studied the effects of *in utero* and lactational exposure to ammonium perchlorate on developing deer mice. Breeding pairs were dosed continuously with 0, 1 nM, 1 µM, or 1 mM of ammonium perchlorate in drinking water, from cohabitation until pups were sacrificed at PND 21. Pups from the second litter were used for evaluation. The researchers found the treated groups tended to have smaller litter sizes than did controls, but a greater survival percentage. They reported that perchlorate is a developmental toxicant and showed variable effects with increasing concentrations. Body weights of the pups in the 1 µM group were consistently lower than in the controls and in other treatments after PND1. They also reported that perchlorate treatment had an effect on the liver and heart weights. However, although liver weight alone was statistically different between treatments, liver weight when analyzed with body weight as a covariate showed no statistically significant difference. Heart weights for male pups were decreased in the 1 µM and 1 mM treatment groups. Heart weights decreased while body weight was increasing. Citing other study results, Thuett *et al.* (2002) suggested that an inadequate level of thyroid hormones during cardiac muscle development can alter cardiac function and/or heart size.

Reproductive Toxicity

Female rats were dosed with perchlorate in drinking water during gestation. The daily intake rates were estimated to range from 237 mg/rat to 615 mg/rat (Brown-Grant, 1966; Brown-Grant and Sherwood, 1971, as cited in U.S. EPA, 2002). These researchers observed no significant differences in litter size, number of pups, and pregnancy rate. Relative thyroid weights of the dams and litters were increased significantly compared with the controls.

A developmental toxicity study was performed on New Zealand White rabbits (Argus Research Laboratories, 1998d). It involved 25 naturally-mated does per group exposed to ammonium perchlorate in drinking water at 0, 0.1, 1.0, 10, 30, and 100 mg/kg-day from gestation day 6 to gestation day 28. Observations were based on 22, 24, 23, 24, 24, and 23 pregnant does that survived to gestation day 29 in the 0, 0.1, 1, 10, 30, and 100 mg/kg-day dosage groups, respectively. Fetuses were delivered by cesarean section. The authors reported that doses as high as 100 mg/kg-day did not affect litter parameters. All values were within the historical ranges of the testing facility. The litter averages for corpora lutea, implantations, litter sizes, live and dead fetuses, early and late resorptions, percent dead or resorbed conceptuses, percent male fetuses and fetal body weights were comparable and did not differ significantly in the six dosage groups.

All placentas appeared normal and no doe had a litter consisting of only resorbed conceptuses (Argus Research Laboratories, 1998d). U.S. EPA (2002) analyzed the maternal hormone data and noted statistically significant decreases in T4 for the 1, 10, 30, and 100 mg/kg-day dose groups. There were no statistically significant changes in T3 or TSH at any dose.

Argus Research Laboratories (1998d) also reported that no fetal alterations (defined as malformations and variations) were attributable to exposure to ammonium perchlorate at doses as high as 100 mg/kg-day: (a) the incidences were not dosage-dependent; (b) the observation occurred in only one or two high dosage group fetuses; or (c) the incidences were within the averages observed historically at the testing facility.

OEHHA notes that rabbit is probably not an appropriate animal model for the study of adverse developmental effects of perchlorate. Studies have shown that the placental iodide transport in rabbit is capable of generating a fetal serum-to-maternal serum iodide concentration of 5/1 to 9/1, thus facilitating the production of fetal thyroid hormone. A similar transport mechanism is not known to exist in human placenta (Hall and Myant, 1956 and Roti *et al.*, 1983, as cited in Fisher, 1996).

In a study by Argus Research Laboratories (2000), female rats were dosed at 0, 0.01, 0.1, 1.0 and 30.0 mg/kg-day ammonium perchlorate in drinking water beginning 15 days before cohabitation and continuing through the day of sacrifice. All rats were sacrificed on gestation day 21, and a gross necropsy of the thoracic, abdominal, and pelvic viscera was performed. Preimplantation loss was noted at all dose levels: 12, 18, 20, 16, and 25 percent at the respective doses from 0 to 30 mg/kg-day. U.S. EPA (2002) noted that it was not clear whether these increases were statistically or biologically significant compared to control animals. OEHHA analyzed the data by the Mann-Whitney U test (since the data are not normally distributed) and found that the increase in preimplantation loss was statistically significant in the 30 mg/kg-day group compared to controls ($p<0.05$). A decrease in the number of live fetuses was also reported to be statistically significant ($p<0.05$) at 30 mg/kg-day, although no significant decrease was noted in the lower dose groups. Ossification sites per litter for sternal centers and forelimb phalanges were significantly reduced at 30 mg/kg-day.

Carcinogenicity

A number of animal studies have been reported that may be useful in determining the carcinogenic potential of perchlorate. However, the interpretation of the study results is hampered by the small number of animals per dose group, short exposure and observation durations, lack of multiple dose groups, and co-exposure to other cancer causing agents.

Gauss (1972) treated female NMRI mice with one percent potassium perchlorate in the diet or the control diet for 160 days. The one percent dose is equivalent to approximately 2,000 mg/kg-day based on standard assumptions. The investigator noted progressive changes in the thyroids of treated mice beginning with colloid loss, progressing to increases in size of nuclei and increased epithelial height, followed by appearance of hyperplasia and hypertrophy of the thyroid parenchyma. Later in the treatment period, hyperplastic follicles, areas of adenomatous tissue, adenoma complexes and secreting cystadenomas were observed. No progression to malignancy was observed during the study period.

Several Japanese investigators (Hiasa *et al.*, 1987) tested potassium perchlorate for its ability to promote the carcinogenic activity of N-bis(2-hydroxypropyl)nitrosamine (DHPN). They divided the rats into four groups. Groups 1, 2, and 3 received 1,000 ppm potassium perchlorate, 1,000 ppm potassium iodide, or 1,000 ppm propylthiouracil in the diet, respectively. Group 4 was the control and received the basal diet throughout the study period of 18 weeks. At the beginning of the study, 50 percent of the rats in each group were injected with DHPN at 280 mg/100 g body weight as an initiator. Rats treated with both chemicals had a 100 percent incidence (20/20) of thyroid adenomas. Rats treated with potassium perchlorate alone had no thyroid adenomas. The incidence was five percent (1/20) in rats given DHPN alone. The investigators concluded that potassium perchlorate promoted the development of thyroid tumors in the rats treated with DHPN, but the chemical itself was not carcinogenic in this experiment.

Groups of male Wistar rats were exposed for two years to zero or one percent potassium perchlorate in their drinking water (Kessler and Kruskemper, 1966). Based on body weights and estimated water consumption, the one percent concentration was estimated to provide a dose of approximately 1,300 mg/kg-day. Animals were sacrificed and examined after 0, 40, 120, 220 and 730 days of exposure. Body weights of control and exposed animals were similar throughout the experiment, but thyroid weights of the exposed rats increased markedly compared to control rats at each examination interval. At 40 days, the exposed rats showed follicular cell hyperplasia, i.e., small follicles with high epithelia, large nuclei, numerous mitoses, colloid resorption and low-grade mesenchymal reaction. According to the authors, these changes are typical of thyroid glands stimulated by TSH for a relatively short time. Diffuse degenerative changes with fibrosis and increased colloid were observed after 200 days. Four of 11 rats treated with one percent potassium perchlorate for two years developed benign thyroid tumors. The twenty untreated controls had no thyroid tumors.

Pajer and Kalisnik (1991) divided 72 female BALB/c mice into 6 groups. Three groups were given 1.2 percent sodium perchlorate in drinking water, while three groups were controls. Eight or 32 weeks after the beginning of the study, one perchlorate and one control group of animals were irradiated with a total of four Grays of ionizing radiation (gamma rays) over a period of five days. Forty-six

weeks after the beginning of the experiment, 42 animals were sacrificed, while 30 had died during the experiment. The perchlorate dose to the treated mice was about 2,100 mg/kg-day based on standard assumptions for body weight and water consumption. Perchlorate treatment alone caused hypothyroidism with hypertrophic and hyperplastic thyroid epithelial cells as well as pituitary thyrotropic cells. Perchlorate and irradiation together caused effects similar to those caused by perchlorate treatment alone. Follicular cell carcinomas of the thyroid gland were found after perchlorate treatment (5/6 mice) and after perchlorate with irradiation (14/14), both statistically significant at $p<0.001$ versus controls (0/22).

The data indicate perchlorate caused thyroid follicular cell carcinomas in the treated mice. The study result is limited by the small number of animals in the perchlorate-only treated group, the design of the study, and the deaths of over 40 percent of the mice before the end of the experiment.

In a two-generation reproductive toxicity study in rats (Argus Research Laboratory, 1998b), two out of 30 male Sprague-Dawley rats (P2) in the highest dose group (30 mg/kg-day) were found to have adenomas of the thyroid. No such tumors were found in the control group or the other dosed groups (0.3 mg/kg-day and 3 mg/kg-day). In the study, the male rats were exposed to ammonium perchlorate in drinking water from conception to 19 weeks of age. As thyroid follicular cell adenomas are relatively rare in male Sprague-Dawley rats (the background incidence of this tumor reported in the literature was only 3.6-3.9 percent), U.S. EPA (2002) concluded that the increase in tumor incidence was treatment related.

In a number of subchronic perchlorate studies, increased thyroid follicular cell hypertrophy and hyperplasia were observed in some of the treated animals (Lampe *et al.*, 1967; Caldwell *et al.*, 1995; Springborn Laboratories, 1998; Argus Research Laboratories, 1998a, 1999, 2001; Keil *et al.*, 1998). Summaries of these studies are provided in sections above. The data indicate that oral administration of perchlorate induces hyperplasia in the thyroid of rodents and if the exposures are lengthened, some of the lesions might progress to thyroid tumors.

Other Toxicities

Acute Toxicity

In acute toxicity testing, animals generally died within the first few days after oral administration of high doses of ammonium perchlorate (750 to 4,200 mg/kg). Autopsy findings included necrosis and hemorrhaging of the mucous membranes of the stomach. Intestinal damage, pulmonary edema, and vascular dilation and congestion of the spleen, brain and sinuses were also noted (Von Burg, 1995).

Table 44, showing acute LD_{50} values for perchlorate salts in several species, is modified from Von Burg (1995), compiled from Schilt (1979), U.S. EPA (1971), Shigan (1963), and Joesten and Hill (1966). The lethal dose for the various perchlorate salts when administered to mice by intraperitoneal injection varied over a 50-fold range.

Mannisto *et al.* (1979) administered potassium perchlorate to male Sprague-Dawley rats in drinking water for four days at concentrations of 0, 10, 50, 100 or 500 mg/L. At the end of the exposure period, they measured blood levels of TSH and thyroid hormones (T3 and T4). Significant changes (increased TSH and decreased T3 and T4) were observed in the 100 and 500 mg/L (15.3 and 76.3 mg/kg-day) exposure groups. In the 50 mg/L (7.6 mg/kg-day) exposure group, there was a significant decrease in concentration of T3 and T4; the TSH level was increased, but the increase was not statistically significant.

Table 44. Acute LD_{50} Values for Perchlorate Salts (Modified from Von Burg, 1995; Schilt, 1979; U.S. EPA, 1971; Shigan, 1963; Joesten and Hill, 1966)

Species	Route of Administration	Cation	Dose (mg/kg)
Rat	Oral	NH_4^+	3,500 to 4,200
Mouse	Oral	NH_4^+	1,900 to 2,000
Rabbit	Oral	NH_4^+	750 to 1,900
Guinea Pig	Oral	NH_4^+	3,310
Mouse	i.p.	Li^+	1,160
Mouse	i.p.	Mg^{++}	1,500
Mouse	i.p.	Na^+	1,150
Mouse	i.p.	Mn^{++}	410
Mouse	i.p.	Fe^{+++}	370
Mouse	i.p.	Co^{++}	160
Mouse	i.p.	Ni^{++}	100
Mouse	i.p.	Cu^{++}	29
Mouse	i.p.	Zn^{++}	76

Genetic Toxicity

Ammonium perchlorate was tested in a battery of genotoxicity tests, and found to be negative in all tests (U.S. EPA, 2002). Ammonium perchlorate was negative in the reverse mutation assay in *Salmonella typhimurium* (TA98, TA100, TA1535, TA1537) with and without S9 activation (ManTech Environmental Technology, 1998). The Ames tests were later repeated by the National Institute of

Environmental Health Sciences. Strains TA102 and TA104 were added to cover the possibility that ammonium perchlorate causes mutation by producing reactive oxygen species or other DNA damaging radicals. The repeat tests also used the pre-incubation test methodology as it provides better contact between the test material and the target organism. Ammonium perchlorate was negative in the reverse mutation assay in *S. typhimurium* (TA98, TA100, TA1535, TA97, TA102, and TA104) with and without S9 activation, thus confirming the original Ames test results (Zeiger, 1998).

Ammonium perchlorate was negative in the L5178Y/TK$^{+/-}$ mouse lymphoma assay without S9 activation. Results of the mouse lymphoma assay with S9 activation were equivocal because of low frequency of mutations in the positive controls (ManTech Environmental Technology, 1998). The test was later repeated. In this assay, concentrations of ammonium perchlorate in the treatment medium of 50 to 5,000 µg/mL were negative in the L5178Y/TK$^{+/-}$ mouse lymphoma mutagenesis assay in the absence and presence of Arochlor-induced rat liver S9 (BioReliance, 1999). The results of the repeat study provided support for the negative results reported in the first study.

Ammonium perchlorate tested negative in *in vivo* micronuclei assays in mice and rats. In the mouse micronucleus assay, five male and five female Swiss CD-1 mice were dosed by gavage at 0, 62.5, 125, 250, 500, or 1,000 mg/kg for three consecutive days. No increases in the frequency of micronuclei were found for any dose group (ManTech Environmental Technology, 1998). There is some uncertainty whether the maximum tolerated dose was reached in the study. Typically, the assay is performed at 85 percent of the maximum tolerated dose, and the 1,000 mg/kg-day dose represents approximately 50 percent of the LD_{50}. Furthermore, there was no indication of toxicity to the bone marrow cells because the polychromatic erythrocyte/normochromatic erythrocyte ratio was not different from the controls. The test was later repeated by the National Institute of Environmental Health Sciences. Male $B6C3F_1$ mice were injected intraperitoneally with 0, 125, 250, 500, 1,000, 1,500, and 2,000 mg/kg ammonium perchlorate in buffered saline. Five mice per group were treated daily for three consecutive days, and were sacrificed 24 hours after the last injection. All animals in the 1,500 and 2,000 mg/kg groups died after the first injection and 4/5 animals in the 1,000 mg/kg group died after the second injection. All animals in the 125, 250, and 500 mg/kg groups survived the treatment. No increases in micronuclei were seen at any of the test doses, and the trend test was not positive (Zeiger, 1999). The negative results of the repeat study support the results of the first study.

The 90-day subchronic bioassay using Sprague-Dawley rats also evaluated micronuclei induction (Siglin *et al.*, 2000). Ten rats per sex were treated with ammonium perchlorate in drinking water for 90 days at 10 mg/kg-day. The results indicate that ammonium perchlorate under the test condition was not mutagenic to the bone marrow cells of male and female Sprague-Dawley rats. The chemical was not toxic to the bone marrow cells at the dose tested, as it did

not reduce the ratio of polychromatic to normochromatic erythrocytes in male or female rats.

Based on the above *in vitro* and *in vivo* genotoxicity test results, ammonium perchlorate does not appear to be mutagenic or clastogenic. Therefore, genotoxicity is not considered a potential mode of carcinogenic action for perchlorate.

Immunotoxicity

Shigan (1963) administered ammonium perchlorate to rabbits and white rats in water at 190 mg/kg-day for three months. The mode of administration was not described. No effect was found on immune function as evaluated by leukocyte phagocytosis (Shigan, 1963).

A series of hematological and immunotoxicology experiments in female $B6C3F_1$ or CBA/J Hsd mice were conducted as part of the U.S. EPA's perchlorate testing strategy (U.S. EPA, 2002). In these experiments, mice were exposed for 14 or 90 days to ammonium perchlorate at doses between 0.02 and 50 mg/kg-day via drinking water. The mice were tested at intervals for immunotoxicological effects such as delayed type hypersensitivity and cytotoxic lymphocyte activity (Keil *et al.*, 1998, 1999; Burleson Research Technologies, 2000).

In the hematological studies, no differences were observed between control and dosed mice in 14- or 90-day experiments for erythrocyte cell count, hemoglobin, hematocrit, mean corpuscular volume, and mean corpuscular hemoglobin concentration, nor in leukocyte differential counts of neutrophils, monocytes, and lymphocytes. An increase in the percentage of reticulocytes was observed in the peripheral blood of mice exposed to 3 mg/kg-day of ammonium perchlorate in a 90-day study. No consistent alteration in the bone marrow stem cell assay was observed. An increase in the number of colony-forming units was observed in bone marrow cell cultures from mice dosed at 30 mg/kg-day in a 14-day study. However, in two other 90-day studies, this positive result was not confirmed. Upon reviewing the immunotoxicological studies, U.S. EPA (2002) found that three immune function parameters were altered by ammonium perchlorate exposure: (a) suppression of *in vitro* peritoneal macrophage phagocytosis of *L. monocytogenes*; (b) enhancement of the plaque-forming cell (PFC) assay response to sheep red blood cells (SRBCs); and (c) enhancement of the local lymph node assay (LLNA) response to 2,4-dinitrochlorobenzene (DNCB).

Decreased *in vitro* phagocytosis of *L. monocytogenes* by peritoneal macrophages obtained from mice dosed for 14 days at 1 or 30 mg/kg-day (ammonium perchlorate) was observed. In mice exposed for 90-days, phagocytosis was decreased in all dose groups (Keil *et al.*, 1998, 1999). However, similar effects were not observed in a 90-day perchlorate exposure followed by a 30-day recovery period study. These *in vitro* data suggest that perchlorate suppresses the phagocytic capacity of peritoneal macrophages, but

this suppression is reversed after a 30-day recovery period. It is difficult to interpret the biological significance of this data set because *in vivo* study results indicate ammonium perchlorate exposure did not alter the ability of mice to combat *L. monocytogenes* infection. It was suggested that while perchlorate may reduce the phagocytic capacity of peritoneal macrophages, the ability of macrophages from other sites (e.g., spleen, liver) to clear *L. monocytogenes* was not altered (U.S. EPA, 2002).

The PFC assay is routinely used for identifying immunosuppressive chemicals. The reason why the highest dose(s) of ammonium perchlorate, given over 90 days, enhanced this response is not known. The enzyme-linked immunosorbant assay (ELISA) data for mice exposed to up to 30 mg/kg-day for 14 or 90 days do not corroborate this enhanced response to SRBCs observed in the PFC assay. The data from Burleson Research Technologies (2000) indicate that exposure to perchlorate enhances the LLNA response to DNCB. While a dose of 50 mg/kg-day for 14 days enhanced the response, the same dose for 90 days suppressed the response. Lower doses of 0.06 and 0.2 mg/kg-day also increased the response; however, interpretation of these data is made difficult by the observation that 2 mg/kg-day did not affect the response in the 14-day study. OEHHA agrees with U.S. EPA (2002) that interpretation of the results is made difficult by (a) some technical problems encountered in the studies, (b) the apparent inconsistency of the high-dose study results, and (c) the unknown biological significance of the response enhancement.

Neurotoxicity

By interfering with the thyroid-pituitary axis, perchlorate can interfere with development of the central nervous system. Thyroid hormone plays an essential role in the development of the corpus callosum and other brain structures. As part of the U.S. EPA's program to evaluate the toxicity of perchlorate, neurodevelopmental tests on Sprague-Dawley rats were conducted by Argus Research Laboratories (1998a; 2001). The study design and findings have been summarized in the "Developmental and Reproductive Toxicity" section.

6. DOSE-RESPONSE ASSESSMENT

Noncarcinogenic Effects

The primary effect of perchlorate exposure is the disruption of thyroid hormone regulation. This mode of action is supported by the results of a number of animal studies that show that perchlorate inhibits thyroidal iodide uptake, changes serum T3, T4, and TSH levels, causes thyroid enlargement, induces thyroid follicular cell hypertrophy and hyperplasia, and a number of other toxicological endpoints, as reviewed in the "Toxicological Effect in Animals" chapter. Similarly, the primary action of perchlorate in humans is inhibition of iodide uptake into the thyroid gland. The function of the thyroid gland is the production of thyroid hormone. Iodide is a key component in the structure of thyroid hormone, and by blocking its uptake into the thyroid, perchlorate can potentially cause decreased production of this hormone. Decreases in thyroid hormone have been associated with impaired neurodevelopment in children, increases in cardiovascular disease risk factors, and other adverse effects.

Selecting the Key Biochemical Effect

In developing PHGs, OEHHA is required by the California Safe Drinking Water Act of 1996 (Health and Safety Code Section 116365) to consider the existence of groups in the population that are more susceptible to adverse effects of drinking water contaminants than are typical healthy adults. The primary mechanism of perchlorate toxicity is inhibition of iodide uptake by the thyroid. Three groups that may be particularly susceptible to this effect of perchlorate due to alterations in iodine status are pregnant women, the developing fetus, infant or young child, or women with low iodine intake.

Thyroid stress of pregnancy: In his review paper, Glinoer (2001) suggested that pregnancy causes profound changes in thyroid function and represents a stress on the thyroid hormonal system. In the first trimester of gestation, there is an increased need for thyroid hormones and an increased need for iodine from the diet. When iodine nutrition levels are sufficient, physiological adaptation takes place. When iodine is restricted or deficient, adequate physiological adaptation is difficult to achieve and is progressively replaced by pathological alterations occurring in parallel with the degree of long-term iodine deprivation. Glinoer concluded, "Therefore, pregnancy typically reveals underlying iodine restriction and gestation results in an iodine-deficient status, even in conditions with only a marginally restricted iodine intake, such as is observed in many European regions."

Results of a prospective study reported by Kung *et al.* (2000) showed that in a borderline iodine-sufficient area (median urinary iodine level = 9.8 µg/dL), pregnancy can pose a stress on the thyroid, resulting in higher rates of maternal

goitrogenesis as well as neonatal hypothyroxinemia and hyperthyrotrophinemia. Thyroid enlargement in these women persisted and failed to revert completely even 3 months after delivery.

Susceptibility of the fetus, infant and young child: As reviewed above, several epidemiological studies provide evidence that iodine deficiency during pregnancy may adversely affect brain development and cause neurointellectual deficits in the offspring. These effects are not limited to areas with severe iodine deficiency and endemic cretinism; effects have been associated with levels of thyroid hormone that fall into what have traditionally been considered normal ranges. The severity of effects may depend on the timing and the severity of the iodine deficiency. In several studies conducted in areas with moderate or even mild iodine deficiency, mainly in southern Europe, it was shown that developmental abnormalities may occur in schoolchildren who are clinically euthyroid. Even borderline iodine deficiency might lead to impaired school performance in some children (Glinoer, 2001).

Since the thyroid is dependent on iodide for thyroid hormone production, inadequate iodine intake can lead to decreased thyroid hormone production. Studies in humans that have identified links between relatively small decreases in thyroid hormone levels during pregnancy and significant effects on cognition in the offspring include Pop *et al.* (1999, 2003), Haddow *et al.* (1999), Klein *et al.* (2001), Kooistra *et al.* (2006), and Vermiglio *et al.* (2004). These findings are supported biologically by animal studies that have linked decreases in maternal thyroxine (T4) during pregnancy to permanent structural changes in the brains of the offspring (Lavado-Autric *et al.*, 2003; Auso *et al.*, 2004; Gilbert and Sui, 2008). Importantly, some of these effects are seen at thyroid hormone levels that are within what has been traditionally defined as the normal range, and in pregnant mothers and offspring without any other evidence of clinical hypothyroidism.

One reason why the fetus, infant or the young child may be particularly susceptible to inadequate iodine intake and small changes in thyroid hormone levels is that the fetal and infant periods are critical times of brain and neurological development. Another reason may be that the fetus and infant do not have fully developed thyroids and have stores of thyroid hormone that are much lower than in adults (van den Hove *et al.,* 1999). These low stores may make them more susceptible to temporary decreases in iodine intake or other factors that may inhibit hormone production. Finally, some data suggest that many young children in the U.S. may not have an adequate iodine intake. Pearce *et al.* (2007) estimated that 47 percent of the breast milk samples in their study of 57 women from the Boston area did not contain enough iodine to meet the infant iodine intake recommended by the Institute of Medicine.

Women with low iodine intake in the U.S.: The rates of most thyroid diseases are much greater in women than in men. The reason for this is unknown, but it suggests that women might be more susceptible to environmentally-caused

thyroid problems than men. In Blount *et al.* (2006), statistically significant associations between increasing perchlorate and decreasing T4 and increasing TSH were seen in women but not in men. In addition, effects on T4 were only seen in women with evidence of somewhat reduced iodine intake (urinary iodine concentrations < 100 µg/L), but not in women with evidence of higher iodine intakes. These effects highlight the importance of gender and iodine status when assessing the potential impacts of perchlorate.

Urinary iodine concentration is an indicator of the adequacy of iodine intake for a population. According to the World Health Organization (WHO), the median urinary iodine concentrations in iodine-sufficient populations should be greater than 100 µg/L (WHO, 1994; as cited in Hollowell *et al.*, 1998). In the NHANES 2001-2, the geometric mean urinary iodine concentration in women was 126 µg/dL, which indicates an adequate iodine intake for the population as a whole. However, this level does not mean that every individual member of the population has an adequate iodine intake. In Blount *et al.* (2006), the perchlorate-T4 association was seen in women with spot urinary iodine levels below 100 µg/L, a group that included 37 percent of all women in the study. The fact that the women in this study were derived from an essentially nationally representative sample of all women in the U.S. suggests that a large number of U.S. women (e.g., 37 percent) have iodine intakes that may put them at risk for effects from perchlorate.

In summary, the primary mechanism of perchlorate toxicity is the inhibition of iodide uptake into the thyroid gland and a subsequent decrease in thyroid hormone production. Iodine deficiency and thyroid insufficiency have been linked to a number of significant adverse health effects including goiter, impaired cognitive development, and increases in cardiovascular risk factors. Some of these links have been seen at levels of iodine and thyroid hormones that have been considered to be within normal reference ranges. OEHHA has chosen to use reduced thyroidal iodide uptake as the key biochemical effect for the perchlorate PHG. This is the same key biochemical effect used in the OEHHA 2004 PHG perchlorate document and the same one used by the NRC in their report on the health implications of perchlorate exposure (OEHHA, 2004; NAS, 2005). The purpose of this PHG is to help prevent any inhibition of thyroidal iodide uptake that could potentially lead to the adverse effects described above.

Selecting the Critical Study

OEHHA used the 14-day perchlorate clinical dosing study of Greer *et al.* (2002) for its dose-response analysis in the 2004 perchlorate PHG document, and five percent inhibition of iodide uptake as the benchmark response (BMR). Greer *et al.* (2002) administered a daily oral dose of perchlorate to groups of male and female volunteers for 14 days at doses of 0.007, 0.02, 0.1, or 0.5 mg/kg-day. Reductions in iodide uptake by the thyroid gland were seen at all four dose levels, with statistically significant reductions at the highest three doses.

In this update, to determine a level of perchlorate exposure that would not inhibit thyroidal iodide uptake, OEHHA again has chosen the Greer *et al*. (2002) study as the critical study and applied the benchmark dose approach for identification of the point of departure. This was selected as the critical study because it was an experimental study in humans where subjects were given known doses of perchlorate and evidence of a dose-response relationship was seen with the key biochemical outcome, iodide uptake in the thyroid. Several other studies have linked perchlorate exposure to changes in thyroid hormones and these were evaluated as to whether they could be used for risk assessment. However, these were either based on ecologic measurements of perchlorate exposure or only a single or few urinary perchlorate measurements (e.g., Kelsh *et al.,* 2003; Blount *et al.,* 2006). Basing exposure on only a few measurements could bias true associations towards the null and lead to an underestimation of true risks. Nonetheless, we estimated a PHG using an analysis of the NHANES data, which is presented in the Appendix. Despite any possible exposure misclassification, this estimate comes quite close to that estimated using Greer *et al.* (2002) data.

Selecting the Point of Departure

The benchmark dose (BMD) is the dose associated with a predefined level of response, the benchmark response (BMR). For this analysis, a five percent decrease of mean radioactive iodide uptake by the thyroid is used as the BMR. A five percent decrease was selected because this is the lowest level of effect that is commonly detectable with statistical significance in many animal and human studies.

A statistical lower bound of the BMD, the 95 percent lower confidence limit (the BMDL), is used as the point of departure for defining an exposure level that is likely to be without an appreciable risk of deleterious effects in humans. Using the BMDL rather than the BMD helps to account for the uncertainty inherent in a given study and according to the U.S. EPA, "assures (with 95 percent confidence) that the desired response is not exceeded" (U.S. EPA, 2000).

U.S. EPA recommends BMD methods to estimate reference doses (RfDs), which are used along with other scientific information to set criteria and standards for noncancer human health effects. In the past, RfDs have mainly been determined from NOAELs, which represent the highest experimental dose for which no adverse health effects have been documented. As noted by U.S. EPA and many others, the BMD approach has several significant advantages over the NOAEL approach when appropriate dose-response data, like those in Greer *et al.* (2002), are available. Using the NOAEL to determine RfDs has long been recognized as having a number of limitations. One is that the NOAEL is limited to only one of the doses in the study and is highly dependent on study design; in particular, the dosages selected by the investigators. In most clinical studies, like Greer *et al.* (2002), only a relatively small number of dose levels are selected. Because the level selected as the NOAEL has to be one of the doses evaluated in the critical

study, the NOAEL is highly dependent on the dose levels chosen by the investigator.

Another weakness is that the NOAEL is highly dependent on the size of the study. The reason for this is that it is usually defined as the highest dose at which there is no *statistically significant* observable effect, and statistical significance is highly dependent on sample size. All else being equal, the larger the sample size, the more likely a finding of a given magnitude (e.g., a 5% decrease in iodide uptake) will be statistically significant. Thus, two studies (one large and one small) may both find the same 5% effect at a particular dose, but this 5% could be statistically significant in the larger study but not in the smaller study. In this example, the 5% effect could be real in both studies, but would be selected as the NOAEL in the smaller study for the sole reason that the investigators did not include more subjects. The same arguments apply to using a NOEL. In the Greer *et al*. (2002) study, a small decrease in iodide uptake by the thyroid was seen in those subjects receiving the lowest perchlorate dose. As seen in Figure 12, the magnitude of this effect is about what was expected based on the magnitudes of the effect sizes seen in the higher dose groups. In a larger study, this may have been statistically significant and considered a LOEL. However, the sample size was small (there were only seven subjects in the lowest dose group), and this small effect size was not statistically significant and thus considered a NOEL. It is possible that this effect was due to chance in Greer *et al*. (2002). However, it is also possible this effect is real or that the actual effect is even higher than observed but ended up being lower due to chance.

In the BMD approach, this is not an issue. This approach involves estimating effect sizes based on the entire dose-response curve, that is, all of the dose levels, all of the sample sizes at each dose level, and all of the effect sizes at each dose level. As such, it is not reliant on any single dose and therefore much less reliant on the doses chosen by the investigator, on the sample size at any single dose level, or the statistical significance of any single result. Sample size is still important in the BMD method in that the results of each dose are partially weighted by the number of subjects at each dose level and in calculating the BMDL.

A final advantage of the BMD approach is that because all dose levels are considered, the shape of the dose-response curve throughout the entire dose range, especially at the lower doses, is taken into account. This can potentially allow for a more accurate estimation of the true effects occurring in the lower dose ranges.

For all of these reasons, OEHHA has chosen to use the BMD approach rather than the NOEL approach. As discussed below, this had only a relatively small impact on the PHG.

Calculation of the BMD Using Greer *et al.* (2002)

OEHHA used the BenchMark Dose Software, version 2.0.0.33 (U.S. EPA, 2008a) to perform the analyses based on the human data reported by Greer *et al.* (2002) shown in Table 45. This is the same analysis, using the same data from Greer *et al.* (2002) that was used in the OEHHA 2004 perchlorate PHG document. A detailed discussion of the application of the software is provided in a U.S. EPA (2012) document, "Benchmark Dose Technical Guidance."

OEHHA tried several curve fitting models provided by the software and found the Hill model adequately describes the data (goodness of fit test, p=0.46), shown plotted in Figure 12. The fit is generally considered adequate when the p-value is greater than 0.10. Other models, including linear and polynomial models, fit the data poorly based on visual inspection and goodness of fit p-values.

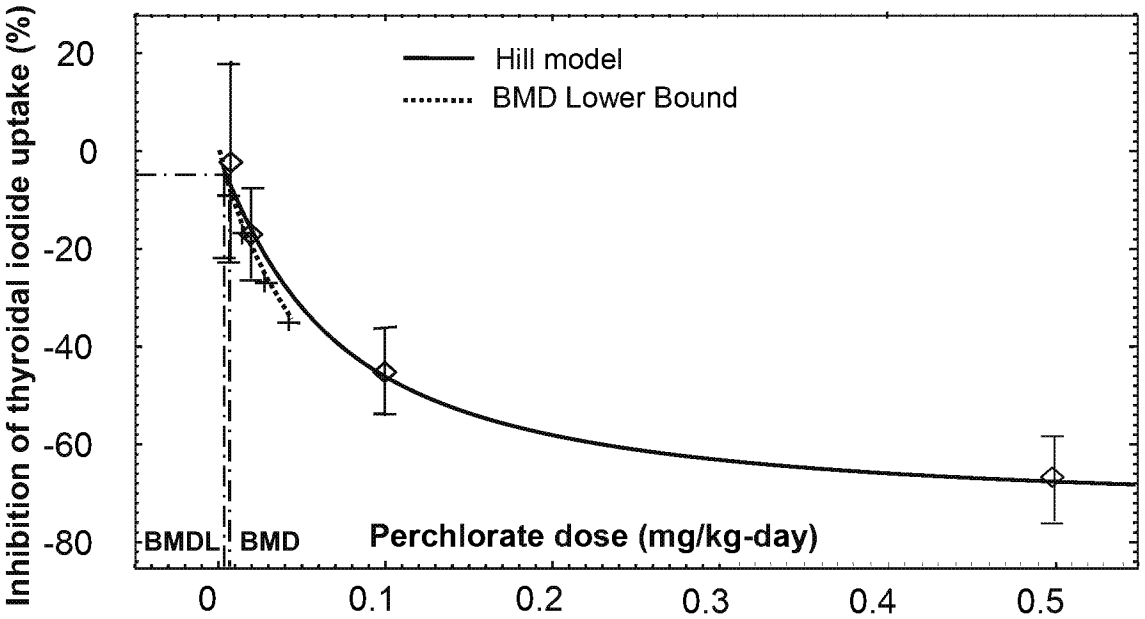


Figure 12. Analysis of the Greer *et al.* (2002) Data by the Benchmark Dose Approach. The Hill model was run with the following settings: intercept = zero, power parameter restricted to be greater than one, a constant variance model assumed. The BMR was a 5 percent decrease in iodide uptake.

The form of the response function estimated by the model is as follows:

$$\text{Response} = \text{intercept} + (v \times \text{dose}^n) / (k^n + \text{dose}^n)$$

where:

intercept = 0
v = -67.076

n = 1.43546
k = 0.0684664

The estimated BMD and BMDL corresponding to a five percent reduction of the mean thyroidal iodide uptake are 0.0068 mg/kg-day and 0.0037 mg/kg-day, respectively. These are the same BMD and BMDL calculated in the 2004 OEHHA perchlorate PHG document. It should be noted that the BMDL of 0.0037 mg/kg-day is lower than the lowest dose tested, 0.007 mg/kg-day, in the Greer *et al*. (2002) study.

Table 45. Human Data from Greer *et al*. (2002)

Average dose (mg/kg-day)	Change in 24 hr radioactive iodine uptake by the thyroid (%)		Number of subjects in each dose group
	Average	Standard deviation	
0.007	-1.844	22.019	7
0.02	-16.393	12.828	10
0.1	-44.693	12.32	10
0.5	-67.076	12.114	10

For comparison, significant changes in serum T3, T4, and TSH levels were observed even at the 0.01 to 0.1 mg/kg-day dose range for perchlorate in adult rodents. Rat fetuses and rat pups are reportedly more sensitive to the effects of perchlorate than adult rats. In several reproductive and developmental studies, colloid depletion of the thyroid, thyroid hypertrophy, and abnormal brain development were found in rat pups exposed to perchlorate *in utero* and after birth. Based on these study results (Springborn Laboratories, 1998; Argus Research Laboratories, 2001), a LOAEL of 0.01 mg/kg-day can be identified.

Carcinogenic Effects

There are two published epidemiological studies that investigated the association between perchlorate in drinking water and cancer (Li *et al*., 2001; Morgan and Cassady, 2002). Based on the reported data, it does not appear that perchlorate was associated with increased risks of cancer in the two study areas during the study periods, under the limitations of the studies.

Several subchronic oral studies in rodents showed that perchlorate induced hypertrophy and hyperplasia in the thyroid gland (Caldwell *et al*., 1995; Springborn Laboratories, 1998; Argus Research Laboratories, 1998b, 1998d, 1999, 2001; Keil *et al*., 1998). In two chronic oral studies, perchlorate at relatively high concentrations (over 1,000 mg/kg-day) was shown to produce thyroid follicular cell tumors in rats (Kessler and Kruskemper, 1966) and mice (Pajer and Kalisnik, 1991). However, only benign tumors were observed in the

study reported by Kessler and Kruskemper (1966), and inadequate reporting and low survival of the control and exposed animals lowered confidence in the results reported by Pajer and Kalisnik (1991). Each study had only one perchlorate exposure group. In a developmental study reported by Argus Research Laboratories (1999), thyroid follicular cell adenomas were also observed in two male Sprague-Dawley rats (2/30) exposed to 30 mg/kg-day perchlorate *in utero* and after birth. No such tumors were found in the vehicle control (0/30). Though the incidence is not significant using standard tests (e.g., Fisher's exact test), the fact that the tumors were found in 19-week old rats and the historical incidence of this type of tumor in male Sprague-Dawley rats in 2-year studies reported in the literature is only 3-4 percent makes the finding noteworthy (U.S. EPA, 2002).

Complex anions structurally similar to perchlorate, such as pertechnetate (TcO_4^-), perrhenate (ReO_4^-) and tetrafluoroborate (BF_4^-), are also capable of inducing thyroid follicular cell neoplasia in test animals (Green, 1978, as cited in Paynter *et al.*, 1988). Based on the limited data available, there are reasons to believe that perchlorate is a potential carcinogen in rodents.

After reviewing thyroid carcinogenesis in rodents and in humans, U.S. EPA (1998b) in the "Assessment of Thyroid Follicular Cell Tumors" stated that "in spite of the potential qualitative similarities, there is evidence that humans may not be as sensitive quantitatively to thyroid cancer development from thyroid-pituitary disruption as rodents. Rodents readily respond to reduced iodide intake with the development of cancer, humans develop profound hyperplasia with "adenomatous" changes with only suggestive evidence of malignancy. Even with congenital goiters due to inherited blocks in thyroid hormone production, only a few malignancies have been found in humans."

One factor that may play a role in interspecies quantitative sensitivity to thyroid stimulation is the influence of protein carriers of thyroid hormones in the blood. In humans, other primates, and dogs a high affinity thyroxine-binding globulin tightly binds T4 (and T3 to a lesser degree); this protein is missing in rodents, rabbits and lower vertebrates. As a result, T4 bound to proteins with lower affinity in the rodent is more susceptible to removal from the blood, metabolism, and excretion from the body. As shown in Table 46, the estimated serum half-life of T4 is much shorter in rats (<1 day) than in humans (5-9 days). This shorter T4 half-life in rats requires a higher level of serum TSH and T4 production rate than in the adult human (U.S. EPA, 1998b). Thus, it appears that the rodent thyroid gland is chronically stimulated by TSH levels above basal levels to compensate for the increased turnover of thyroid hormones, and this in turn could move the gland towards increased growth and potential neoplastic change more readily than in humans. It is interesting to note that adult male rats have higher serum TSH levels than females, and they are often more sensitive to goitrogenic stimulation and thyroid carcinogenesis. In humans, there is no sex difference in hormone levels, but females much more frequently develop thyroid cancer (U.S. EPA, 1998b).

Some of the studies summarized in this document provide some evidence of a quantitative difference in the thyroid responses of humans and rodents to perchlorate, based on applied dose. Several 14-day drinking water studies showed significant depression in serum T3, T4, and elevation in serum TSH levels in rodents exposed to doses as low as 0.01 or 0.1 mg/kg-day (Caldwell *et al.*, 1995; Springborn Laboratories, 1998; Keil *et al.*, 1998; Yu *et al.*, 2000). By contrast, serum T3, T4, and TSH levels in healthy adult humans that are not iodine deficient are much less sensitive to perchlorate exposure. For instance, after exposure to perchlorate in drinking water as high as 12 mg/kg-day for 1, 2, or 4 weeks, no significant changes in serum T3 and T4 levels were found in male volunteers. Serum free T4 and TSH levels were significantly depressed following perchlorate exposure when compared to those before exposure (Brabant *et al.*, 1992; Mattie, 2000). A significant reduction in intrathyroidal iodine concentration was also noticed in the study reported by Brabant *et al.* (1992). Lawrence *et al.* (2000) found no change in serum T3, T4, and TSH in male volunteers exposed to perchlorate in drinking water at 0.14 mg/kg-day for 1 and 2 weeks. Greer *et al.* (2002) exposed male and female volunteers to perchlorate in drinking water at 0.02, 0.1, or 0.5 mg/kg-day for 2 weeks and collected blood samples on days 1, 2, 3, 4, 8, and 14. Statistically significant depression of iodide uptake by the thyroid was observed in the upper two dose groups. However, no significant depression in serum T3 and T4 nor elevation in serum TSH was observed. No dose-response relationships were noticed for these thyroid and pituitary hormones. These data show that though a similar mode of action of perchlorate is operative in rodents and humans, the sensitivities of serum T3, T4, and TSH levels of the two species to perchlorate may not be the same. However, this remains to be fully elucidated. Greer *et al.* (2002) and the other clinical studies cited above only evaluated healthy adults, not sensitive members of the human population such as pregnant women and their fetuses, women with low iodine status, people with thyroid disease, or infants. There is some epidemiological evidence that lower levels of chronic perchlorate exposure seen in the NHANES data (Steinmaus *et al.,* 2010) affect newborn thyroid function.

Table 46. Inter- and Intraspecies Differences of T3, T4, and TSH Levels and Sensitivity to Thyroid Cancer (Modified from U.S. EPA, 1998b)

Parameter	Human	Rat
Thyroxine-binding globulin	Present	Essentially absent
T4 half-life	5-9 days	0.5-1 day
T3 half-life	1 day	0.25 day
$\frac{\text{T4 production rate}}{\text{kg body weight}}$	1 ×	10 × that in humans
TSH	1 ×	6-60 × that in humans
Follicular cell morphology	Low cuboidal	Cuboidal
Sex differences		
Serum TSH	Sexes equal	Male $\leq$ 2 × Female
Sensitivity to thyroid cancer	Female = 2.5 × Male	Male > Female

In evaluating a thyroid carcinogen, it is important to determine the mode of action as it impacts the choice of models in high-to-low dose extrapolation. In the "Assessment of Thyroid Follicular Cell Tumors," U.S. EPA (1998b) stated that in order to show the antithyroid activity of a chemical is the cause of thyroid tumors observed in rodents, it is necessary to demonstrate the following:

1. Increases in thyroid growth;
2. Changes in thyroid and pituitary hormones (considered to be the most important);
3. Location of the sites of antithyroid action (documents where in the body the chemical under assessment leads to perturbations in thyroid-pituitary function);
4. Dose correlations among various effects (to determine where the growth curve for the thyroid gland deviates from the normal pattern of cell replacement and how this relates to doses producing tumors); and
5. Reversibility of effects following treatment cessation during the early stages of disruption of the thyroid-pituitary axis (shows that permanent, self-perpetuating processes have not been set into motion).

The available toxicity data of perchlorate appear to have fulfilled the five requirements described above. Several *in vitro* and *in vivo* genotoxicity studies have been performed on perchlorate. Under the testing conditions, none of the tests indicates perchlorate is a genotoxic agent. Perchlorate is known to inhibit the uptake of iodide in the thyroid, thereby causing a reduction in the hormones T3 and T4. Subchronic and chronic drinking water studies showed that perchlorate exposure depressed serum T3 and T4 but elevated serum TSH

levels in rodents and rabbits. At higher exposure levels, thyroid follicular cell hypertrophy, thyroid follicular cell hyperplasia, and increased thyroid weights were also observed in adults as well as postnatal rats, as described in the chapter "Toxicological Effects in Animals."

There is also evidence that the thyroid follicular cell hypertrophy and hyperplasia observed in rats exposed to ammonium perchlorate might be reversible. In the study reported by the Springborn Laboratories (1998), absolute and relative thyroid/parathyroid weights were significantly increased in male rats exposed to 10 mg/kg-day for 14 days as well as 90 days. However, no significant increases in both absolute and relative thyroid/parathyroid weights were observed in male rats exposed to 10 mg/kg-day for 90 days, followed by a 30-day recovery period. Similarly, absolute and relative thyroid/parathyroid weights were significantly increased in female rats exposed to 10 mg/kg-day for 90 days, but no significant increases in terms of both absolute and relative thyroid/parathyroid weights were observed in female rats exposed to 10 mg/kg-day for 90 days, followed by a 30-day recovery period.

The available data suggest that thyroid tumors observed in rodents exposed to perchlorate via the oral route are likely to be caused by the disruption of thyroid-pituitary homeostasis. It follows that if there were no thyroid and pituitary hormone changes, and no thyroid follicular cell hypertrophy and hyperplasia, there would be no thyroid tumors. For this reason, the perchlorate dose determined for prevention of a detectable decrease in T4 in humans (noncarcinogenic effect) is reasoned to be protective against thyroid tumors as well.

There are no adequate data from human studies to evaluate the cancer potency of perchlorate. Several studies in laboratory animals have reported increases in thyroid tumors following perchlorate exposures, although these have involved doses that are orders of magnitude higher than the exposure levels seen in the dose-response data OEHHA used for BMD modeling. Furthermore, there are difficulties in estimating the cancer potency of perchlorate based on animal cancer data because of differences in iodine deficiency and thyroid disease status (background rates) in laboratory animals compared to humans. For these reasons, a quantitative dose-response evaluation was not performed for the possible carcinogenic effects of perchlorate. It is reasoned that by setting the perchlorate PHG low enough to avoid impacts on thyroid hormone status, all other potential adverse thyroid effects, including benign and malignant thyroid tumors, will be prevented.

7. CALCULATION OF THE PHG

The PHG is derived in this section by first calculating an Acceptable Daily Dose, or maximum amount that can be consumed without toxic effects, using the BMD value derived from the human study by Greer *et al.* (2002) in the last chapter. This is then converted into an acceptable drinking water perchlorate concentration. In making these calculations, population subgroups that may be much more susceptible to the effects of perchlorate than healthy adults and perchlorate exposures from sources besides drinking water are taken into account. The resulting updated PHG will help prevent perchlorate-related reductions in thyroidal iodide uptake and subsequent decreases in thyroid hormone production that may be associated with adverse health effects.

A quantitative dose-response evaluation was not performed for the possible carcinogenic effects of perchlorate. By setting the perchlorate PHG low enough to avoid impacts on thyroid hormone status, all other potential adverse thyroid effects, including benign and malignant thyroid tumors, are assumed to be prevented.

Acceptable Daily Dose (ADD)

For estimation of a health-protective concentration of perchlorate in drinking water, an acceptable daily dose (ADD) of the chemical from all sources will first be calculated. This involves incorporation of appropriate estimates of uncertainty in the extrapolation of the dose leading to the key biochemical effect from human or animal studies to the estimation of a lifetime ADD that is unlikely to result in or lead to any toxic effects. For this purpose, the following equation can be used:

$$\text{ADD} = \frac{\text{NOAEL/LOAEL/BMDL in mg/kg-day}}{\text{UF}}$$

where,

ADD = estimated maximum daily dose that can be consumed by humans for an entire lifetime without toxic effects;

NOAEL/LOAEL/BMDL= no-observed-adverse-effect level, lowest-observed-adverse-effect level, or lower limit on the benchmark dose estimated from the critical study;

UF = uncertainty factor(s).

For this case, OEHHA chose to estimate the ADD from the lower limit of the two-sided 95 percent confidence interval of the perchlorate dose estimated to cause a five percent reduction in iodide uptake in the thyroid gland based on the findings of Greer *et al.* (2002).

An uncertainty factor of 10 is applied to help account for interindividual variability in the population that was not captured by the Greer *et al.* (2002) study. This factor is used to account for uncertainty in interindividual differences in toxicodynamic and toxicokinetic factors that may impact susceptibility. It is not intended to account for drinking water intake rates and actual estimates of perchlorate intake and exposure, which are incorporated separately. The Greer *et al.* (2002) study included only 37 healthy adults so the variability of the study data is likely to be smaller than that in the general population. Furthermore, the study population did not specifically examine individuals with low iodine intake, pregnant women, infants, or with the other potential susceptibility factors. Potentially susceptible groups include:

- Neonates and infants, who may be susceptible to perchlorate for several reasons:

    a. Infancy is a critical period for development of the brain and nervous system, processes that are critically reliant on adequate supplies of thyroid hormone. The role that thyroid hormone plays in these critical developmental processes highlights the potential importance of any agent, like perchlorate, whose mechanism involves alterations in thyroid hormone production.

    b. Some data suggest that neonates have stores of thyroid hormone and iodide that are much less than those in adults (Van den Hove *et al.*, 1999). This would make neonates less able than adults to respond to any factor that temporarily decreases iodine intake, iodide uptake, or thyroid hormone production.

    c. Data from several studies (Kelsh *et al.,* 2003; Brechner *et al,.* 2000; Steinmaus *et al.,* 2010; and others) provide evidence of a possible link between perchlorate in drinking water during pregnancy and thyroid hormone levels in newborns.

    d. Preterm infants may be the subgroup most at risk for impairment in thyroid hormone production caused by a reduction in iodine intake or iodide uptake by the thyroid. Intrathyroidal stores of thyroid hormone and iodide are markedly less in preterm infants than in full term infants (van den Hove 1999). In addition, preterm infants have immature pituitary-thyroid function, and lose the contribution of maternal thyroid hormone at birth. Preterm infants also can have immature gastrointestinal function which could reduce their iodine intake.

    e. Since the primary mechanism of perchlorate toxicity is reduced iodide uptake by the thyroid, individuals who are already iodine deficient may be particularly susceptible to perchlorate toxicity. Importantly, the breast milk of many women may not provide an adequate iodine intake for the breast-fed child.

- Women with low iodine intakes. In Blount *et al.* (2006), statistically significant associations between increasing perchlorate and decreasing T4 were seen in women with urinary iodine levels below 100 µg/L, but not in women with higher iodine levels. Estimates from NHANES 2001-2 suggest that 37 percent of all women in the U.S. have urinary iodine levels below 100 µg/L (Blount *et al.*, 2006).

- The developing fetus. Studies have shown that decreases in maternal T4 during pregnancy, even relatively small ones, can lead to significant cognitive deficits in the offspring.

- Lactating women. Lactating mothers are considered a potentially sensitive subpopulation for effects of perchlorate because their need for iodine is greater than other adults. They are therefore at greater risk of getting an insufficient amount of iodine from the diet. The NAS (2001) suggests an Estimated Average Requirement and a Recommended Dietary Allowance of iodine almost two-fold higher for lactating mothers than for other adults.

- Pregnant women, who also have increased iodine requirements.

- People with thyroid diseases.

- People with high levels of thiocyanate, which typically comes from food or tobacco smoking. Data from Steinmaus *et al.* (2007) suggest that the magnitude by which perchlorate reduces T4 levels is about two times greater in people with high thiocyanate levels than in people with average or low thiocyanate levels (Table 40).

In summary, an uncertainty factor of 10 is applied to account for all sensitive groups, including infants, who may be more susceptible to perchlorate than the 37 healthy research volunteers in Greer *et al.* (2002). OEHHA notes that the uncertainty factor of 10 that used here is the same as the uncertainty factor of 10 recommended and used by the NRC to calculate its most recent perchlorate reference dose for U.S. EPA (NAS, 2005).

OEHHA considered an additional uncertainty factor of three to account for the short duration of the Greer *et al.* (2002) study. However, there is evidence in this study that iodide uptake is inhibited fairly quickly after exposure begins and the inhibition does not increase or increases only slightly as exposure continues. That is, in the three highest dose groups (those in which statistically significant reductions in iodide uptake were seen), the greatest proportion of the inhibition occurred by the second day of dosing and either did not worsen or worsened only slightly by day 14 of dosing. Furthermore, it can be argued that if there is no reduction in thyroidal iodide uptake, there will be no concomitant reduction in stored iodide, and extending the exposure duration is not likely to have an impact on the thyroid function. For this reason, OEHHA decided against an additional factor to account for the short duration of the critical study.

Given an uncertainty factor of 10 to account for increased susceptibility in infants,

$$\text{ADD} = \frac{3.7\ \mu g/kg\text{-}day}{10} = 0.37\ \mu g/kg\text{-}day$$

Public Health Protective Concentration (C)

Calculation of the updated public health protective concentration (C) for perchlorate in drinking water uses the following equation for noncarcinogenic endpoints:

C = ADD µg/kg-day × (BW/WC) × RSC

where:

(BW/WC) = the ratio of body weight (kg) and tap water consumption rate (L/day); the ratio for the 95th percentile of infants age 0-6 months is estimated to be 4.2 kg-day/L (OEHHA, 2012; Table 47); and

RSC = relative source contribution. A value of 0.73 (73 percent from water) is used to account for exposure of infants to perchlorate in their diet.

The 95th percentile water consumption rate and body weight ratios are based on water intake estimates derived by OEHHA (2012). These rates were based on data from the Continuing Survey of Food Intake of Individuals (CSFII) for the years 1994-1996, 1998. The CSFII was a large multistage probability sample collected by the U.S. Department of Agriculture involving over 20,000 individuals from throughout the U.S. The CSFII survey collected data on food and beverage intakes for two 24-hour non-consecutive periods, 3-10 days apart. These data were based on recall of dietary and water intake information, and it is possible that intake is overestimated in some people, and underestimated in others. These errors could balance each other out. Overall, their true impact is unknown although there is no reason to believe they were large. Because these data are based on the average of two separate assessments of drinking water intake in each individual collected 3-10 days apart, they are more likely to represent true longer-term intake patterns than data collected using a single day survey.

Using the CSFII data, the U.S. EPA Office of Water estimated the amount of water consumed by each individual (U.S. EPA 2004). For all demographic groups except infants, this included both water consumed directly from the tap for drinking (direct water) and water from the tap used to prepare beverages and foods, either at home or at a food service establishment (indirect water). OEHHA used these U.S. EPA estimates for those subjects reported to be drinking water consumers only since these are the people most likely to have the greatest exposures from local public drinking water sources (OEHHA, 2012).

For infants, OEHHA also used data from the CSFII but derived water intake rates based on the water used by infants consuming reconstituted formula. In order to identify infants who received reconstituted formula, OEHHA reviewed the food descriptions provided for the formula consumed by each infant in the CSFII. The amount of reconstituted formula consumed was then multiplied by the percent of indirect water in each type of reconstituted formula in order to calculate the amount of water consumed by each infant. Sample weights provided in the CSFII dataset were used to weight each individual's intake according to the number of infants in the population that he/she represented and these data were used to calculate distributional characteristics including 95th percentiles. The 95th percentiles rather than the means or medians were used to calculate the health protective concentration since this accounts for the fact that some people have much higher drinking water intake rates (and thus much higher intake of chemicals in their drinking water) than others. Further details and justification of these estimates are provided by OEHHA (2012).

Water intake rates for the various population groups used to calculate health-protective concentrations are shown in Table 47. OEHHA is focusing on infants in these calculations based on the variety of data discussed above showing that this group may be particularly susceptible to perchlorate. This includes the studies from California and elsewhere that provided evidence that thyroid hormone levels in infants were adversely affected by relatively low perchlorate exposure levels (Kelsh *et al.,* 2003; Brechner *et al*., 2000; Buffler *et al.,* 2006; Steinmaus *et al*., 2010; Li *et al.,* 2000a; Crump *et al.,* 2000). It also includes the data discussed above suggesting that many infants may not be receiving adequate iodine in their diets and that young infants have low stores of thyroid hormone (less than one day's worth compared to several weeks' worth in adults) (van den Hove *et al*., 1999; Pearce *et al.,* 2007). In addition, formula-fed infants have much higher water intake rates than older children and adults. Thus, their exposure to perchlorate from drinking water on a body weight basis at a given perchlorate concentration in drinking water will be considerably higher than in children or adults.

Food and water are the primary sources of exposure to perchlorate for most people. Perchlorate has been detected in a wide variety of foods, including fruits, vegetables, grains, dairy milk, and human breast milk (Kirk *et al*., 2005; Pearce *et al*., 2007; Murray *et al*., 2008). Perchlorate levels in urine from NHANES 2001-2, as reflected in the analysis of Blount *et al*. (2006), are generally supportive of the analysis of estimated intakes of perchlorate from foods provided by the U.S. FDA (U.S. FDA, 2009). Together, these data demonstrate that food is the primary source of perchlorate for the general population.

Estimates of perchlorate intake from food were derived from the U.S. FDA's Total Dietary Survey 2005–2006 as reported in U.S. EPA, 2008b. The RSC was defined as the proportion of the ADD not derived from food, and was calculated using the following equation:

RSC = (ADD – estimated perchlorate intake derived from food) / ADD

For most adults, including pregnant and lactating women, the mean perchlorate intake from food was estimated to be 0.10 µg/kg-day. At an ADD of 0.37 µg/kg-day, the RSC then equals 0.73, or 73 percent of the acceptable dose available for consumption in tap water.

The U.S. FDA Total Diet Survey did not provide information on perchlorate intake in infants less than 6 months old. In addition, this survey did not report estimates of perchlorate intake in analyses that only included infants who are formula-fed. Since the intake of perchlorate from food in formula-fed infants could be substantially higher than that in breast-fed infants, failure to specifically evaluate this group could have resulted in a PHG that was not adequately protective in formula-fed infants. Schier *et al.* (2010) measured perchlorate concentrations in 15 different powdered infant formulas (using perchlorate free water) and calculated mean perchlorate intake values based on the estimated daily ingested volume of formula. Perchlorate concentrations in formula varied by formula type and ranged from 0.03-5.05 µg/L, and the estimated geometric mean intake of perchlorate from the different formula types ranged from 0.03 to 0.29 µg/kg-day, with an average of 0.10 µg/kg-day. Using this average and the equation above, an RSC of 0.73 is also estimated for infants.

Using this RSC, the health-protective concentration (C) for infants is estimated to be:

C = 0.37 µg/kg-day x 4.2 kg-day/L x 0.73
C = 1.13 µg/L = 1 µg/L (ppb) (rounded)

Table 47 shows the values of C calculated for infants compared to those for other subpopulations. A relative source contribution of 73 percent and an uncertainty factor of 10 were used in all calculations.

Table 47. Estimated Health Protective Water Concentrations (C) of Perchlorate for Various Subpopulations, Assuming Intakes of Perchlorate in Food of 0.10 µg/kg-day[a] and an RSC of 0.73[b]

Group	Drinking Water Intake (L/kg-day)[c]	BW/WC (kg-day/L)	C (µg/L)
Infants (< 6 months old)	0.237	4.2	1.13
Pregnant women	0.043	23.3	6.29
Lactating women	0.055	18.2	4.92
Females (age 15-44)	0.038	26.3	7.10
Adults (16+)	0.045	22.2	6.00

[a]Based on estimated adult intakes using data from the 2005-6 U.S. FDA Total Dietary Study (U.S. EPA, 2008b) and infant intake from the data of Schier *et al.* (2010).
[b]Calculated as: (ADD – estimated food perchlorate intake) / ADD).
[c]95th percentile intake for drinking water consumers including both direct and indirect water for groups other than infants. For infants, drinking water intake is based on water used to reconstitute infant formula (OEHHA. 2012).

Based on these estimates, OEHHA calculated a PHG of 1 ppb (µg/L). OEHHA concludes that this level is health protective for lifetime exposure to perchlorate in drinking water, and is protective of sensitive populations including infants, pregnant women and their fetuses, those with low intake of iodine or high intake of other thyroid iodide uptake inhibitors, and other potentially susceptible groups.

A benchmark dose analysis was also done using the NHANES 2001-2 data discussed above (Blount *et al.,* 2006), and this provided results similar to those obtained using the Greer *et al.* (2002) data (see Appendix). The NHANES 2001-2 analysis required several data transformations, which greatly increased its complexity. The analysis using the Greer *et al.* (2002) data was used to calculate the final updated PHG since it is an experimental study where exposure levels are known for more than just a single point in time.

8. RISK CHARACTERIZATION AND CONCLUSION

Exposures to Perchlorate

In NHANES 2001-2, an essentially nationally representative sample of people ages ≥12 years in the U.S., perchlorate was detected in the urine of every one of the 2,820 people tested (Blount *et al.*, 2007). This suggests that probably everyone in California, as well as everyone in the U.S., is exposed to perchlorate through some source.

The primary routes of exposure are through food and water. In a recent study by the U.S. FDA, perchlorate was found in many commonly consumed foods including dairy products, fruits, and vegetables (U.S. FDA, 2009). In fact, perchlorate was detected in at least one sample of over 70 percent of the individual food items tested. The U.S. EPA recently estimated that as many as 16.6 million people in the U.S. may be drinking water with perchlorate concentrations greater than 4 ppb (U.S. EPA, 2008a). In California, from 2010 to 2013, detectable levels of perchlorate were reported in 248 public drinking water sources (Table 2) (SWRCB, 2014). The Colorado River is also known to be contaminated with perchlorate, and this water source is used by several large public drinking water agencies in California. For both the U.S. EPA and the California SWRCB surveys discussed above, analyses were based on detection limits of 4 ppb, and it is possible that millions more people are exposed at levels below this. This highlights the potential widespread perchlorate exposure in California that may be occurring from public drinking water sources.

Currently, the actual number of people that are likely to be affected by perchlorate from public drinking water in California is unknown. However, given the data above suggesting that hundreds of public water sources in California contain perchlorate, and given that potential susceptible groups including infants and women with low iodine intake represent a large fraction of the entire population, the number of people that may be affected by perchlorate exposure through their public water supplies is likely to be quite large.

Perchlorate in water can be naturally occurring as well as a result of industrial contamination. The fact that it can occur naturally does not decrease the potential health consequences of exposure. Many naturally occurring chemicals such as arsenic, lead, and asbestos are also toxic and measures are taken to reduce human exposures. Thus, the PHG is based on perchlorate exposure in drinking water whether its presence is due to natural or man-made events.

Health Impacts of Perchlorate

There is a continuum in the possible health effects from perchlorate exposure resulting from its effects on the thyroid, and some susceptible groups or individuals may have perchlorate-related effects at exposures that are lower than those causing similar effects in healthy individuals. For fetuses, infants and children, there is the potential for abnormal growth and development. Of particular concern are effects on brain development. Decreases in thyroid hormone production in infants are related to decreases in IQ. Much of the knowledge on the potential effects of perchlorate comes from extensive data on iodine deficiency in humans.

OEHHA considers effects on thyroid hormone production and subsequent changes to be adverse. Iodide uptake inhibition is the key event that leads to other possible effects from perchlorate exposure. Prevention of iodide uptake inhibition prevents progression to the adverse health effects of perchlorate. The inhibition of iodide uptake by perchlorate has been clearly documented in humans. The National Academy of Sciences (NAS, 2005) deemed "inhibition of iodide uptake by the thyroid as the basis of the perchlorate risk assessment to be the most health-protective and scientifically valid approach." OEHHA agrees with this approach and used it in developing its original 2004 PHG for perchlorate.

The Greer *et al.* (2002) study was used to characterize perchlorate's inhibition of iodide uptake for both the current PHG and the 2004 PHG. It might be argued that the magnitudes of the effects seen in the Greer *et al.* (2002) study were relatively small, and might not be noticeable in otherwise healthy individuals. However, this ignores the impact of these effects on a population basis. Any downward shift in the mean level of the thyroid hormone T4 in a population could increase the number of people who fall into the range of T4 values that are associated with high risks of either subtle or overt thyroid-related disease and toxicity (Miller *et al.,* 2009).

The purpose of the perchlorate PHG is to identify a level of perchlorate in drinking water that prevents any perchlorate-related reduction in thyroid iodide uptake that might lead to decreases in thyroid hormone production. Evidence suggests that even small decreases in thyroid hormone levels may be associated with significant adverse effects, including altered cognitive development in children and increased cardiovascular risk factors in adults. Importantly, these changes have been seen at thyroid hormone levels that are within what have been traditionally defined as normal reference ranges, and have occurred in people without any other evidence of overt thyroid disease. These findings suggest that small changes in thyroid hormone levels may be associated with at least some increased risk of thyroid-related adverse outcomes.

Health Value for Perchlorate from the Greer et al. (2002) Study

OEHHA used the BMD approach rather than the no-observed-effect level (NOEL) approach for the following reasons. OEHHA, like U.S. EPA, has chosen to use the BMD approach as the standard method in dose calculations, provided there are sufficient data to do so. As the U.S. EPA (2012, p. viii) notes, the BMD approach "involves dose-response modeling to obtain BMDs, i.e., dose levels corresponding to specific response levels near the low end of the observable range of the data, incorporates and conveys more information than the [NOAEL; no-observed-adverse-effect level] or [LOAEL; lowest-observed-adverse-effect level] process traditionally used for noncancer health effects." The NAS (2009, p. 129) in its review of U.S. EPA risk assessment practices similarly has recognized this as a refinement that makes better use of the dose-response evidence available than do calculations based on NOAELs.

The NOEL approach depends heavily on a single chosen dose level used in a study, and how closely it is placed relative to the next highest dose. The NOEL approach treats small and large studies the same, even though small studies, with their limited number of subjects, are less likely than large studies to find health effects at any given dose. In this case, the small group sizes in the Greer *et al*. (2002) study make it more difficult to detect an effect. For these reasons reliability of the NOEL approach can vary depending on the size of the study. In contrast, the BMD approach provides a systematic method for calculating a dose at a low specific effect level. The BMD approach uses all the dose-response evidence in the study, incorporates the shape of the dose-response curve, and takes into account the number of subjects in the study, thus providing a more reliable calculation. The advantages of using the BMD approach for this PHG are particularly important given the limited number of subjects that participated in the Greer *et al*. (2002) study.

Identifying Infants as a Sensitive Population

OEHHA, as part of its periodic review of perchlorate, assessed exposure patterns in bottle-fed infants as well as the special susceptibility of infants and children. OEHHA determined that infants, along with pregnant women and fetuses, are likely to be more susceptible to the effects of perchlorate.

The major change in the current PHG calculation relates to the updated information on infants as a sensitive population. OEHHA's review and updating of the perchlorate PHG considered the data from several human studies published after the 2004 PHG and the 2005 NAS review. These studies provided qualitative support for recognizing that infants are likely to be significantly more susceptible to perchlorate than healthy adults. Evidence for this includes the following:

1. New data suggest that many infants may not be receiving adequate iodine in their diets. In a study of nursing mothers in Boston, 47 percent of breast milk samples did not contain enough iodine to meet the infant iodine intake recommended by the Institute of Medicine (Pearce *et al.,* 2007). Perchlorate-related toxicity is likely to be greater in infants who are already deficient in iodine.
2. OEHHA's analysis of data from studies conducted in California and elsewhere provide evidence that thyroid hormone levels in infants were adversely affected by perchlorate at exposure levels that were much lower than the levels shown to cause no effects in healthy adults (Kelsh *et al.,* 2003; Brechner *et al*., 2000; Buffler *et al.,* 2006; Steinmaus *et al*., 2010; Li *et al.,* 2000a; Crump *et al.,* 2000).
3. Young infants have low stores of thyroid hormone (less than one day's worth, compared to several weeks' worth in adults) (van den Hove *et al*., 1999). Because of these low stores, infants may be less able to tolerate transient periods of decreased iodide uptake and decreased thyroid hormone production compared to adults.
4. Human data suggest that perchlorate can interact with other contaminants to produce a greater effect than that caused by perchlorate alone (Blount *et al*., 2006; Steinmaus *et al*., 2007), and infants are exposed to these same contaminants.

In the 2004 PHG, an uncertainty factor of 10 was applied to address all sensitive groups (pregnant women, lactating women, thyroid compromised adults) except infants, where an uncertainty factor of 3 was used. However, given the evidence discussed above, the extent and ways infants are likely to be more susceptible to perchlorate than healthy adults, and the fact that the Greer *et al.* (2002) study included only healthy adults, OEHHA has increased the uncertainty factor applied to infants from the factor of 3 used in the 2004 PHG to a factor of 10 in this updated PHG. This is one factor that resulted in the lowering of the updated PHG. The other factor driving the change in the PHG value is the use of updated drinking water intake rates for infants, described below.

Water Consumption by Infants

The water consumption rate by infants is one of the factors that influence the final PHG. The recent analysis by OEHHA (2012) of data available from a large survey of food and beverage intake conducted by the U.S. Department of Agriculture shows that drinking water intakes per kilogram of body weight are higher in infants than previously thought. This means that infants are likely to have greater perchlorate exposure per kilogram of body weight for a given concentration of perchlorate in drinking water than was estimated in the 2004 PHG.

OEHHA used its new analysis and chose the 95th percentile drinking water intake rate instead of an average rate in order to protect the infant population,

and not just those with average drinking water consumption. Infants who drink more water will have a greater exposure to perchlorate and thus may be at greater risk. In this case the bottle-fed infant will have the greatest intake of water and exposure to water contaminants.

The 95th percentile value of 0.237 L/kg-day for drinking water intake per body weight for infants aged 0-6 months (OEHHA, 2012) was used in the PHG calculations. For comparison, U.S. EPA (2009) typically assumes that infants and children drink 1 liter (L) per day and that they weigh 10 kilograms, that is 0.1 L/kg-day. Using the U.S. EPA value would result in a PHG of 2.7 ppb instead of 1 ppb.

Comparison with Other Agencies

Currently, there is no federal drinking water standard (MCL) for perchlorate. The current California MCL is 6 ppb. Several other states have action levels or MCLs in the range of 1-26 ppb as shown in the table below.

Table 48. State MCLs or Advisory Levels (ppb) for Perchlorate (ASTSWMO, 2011)

Alabama	24.5	Missouri	10.9
Alaska	26	New Jersey	5
Arizona	14	New Mexico	1
California	1 (PHG) 6 (MCL)	New York	5
Florida	4	Nevada	18
Hawaii	25	North Carolina	2
Kansas	10.9	Texas	17
Maine	1	Vermont	2 (prevent) 4 (enforce)
Maryland	1	Virginia	15
Massachusetts	2	Wisconsin	1 (prevent) 0.1 (enforce)

PHGs published by OEHHA are for use by the California State Water Resources Control Board (SWRCB) in establishing primary drinking water standards, that is, the California MCLs. In developing the PHG for perchlorate, OEHHA's approach follows that used by the NAS (2005) to develop its reference dose in several key areas:

1. Both OEHHA and NAS identified the Greer *et al.* (2002) human study as the critical study for evaluating the effects of perchlorate.
2. Both OEHHA and NAS chose iodide uptake inhibition in the Greer *et al.* (2002) study as the key effect on which to base their calculations.
3. Both OEHHA and NAS noted that the subjects in the Greer *et al.* (2002) study were healthy adults and concluded that some people may be more

susceptible to perchlorate than these healthy adult subjects. For this reason, both OEHHA and NAS applied an uncertainty factor of 10 to calculate a dose that would address inter-individual variability among humans and be protective of those who are likely to be sensitive to the effects of perchlorate.

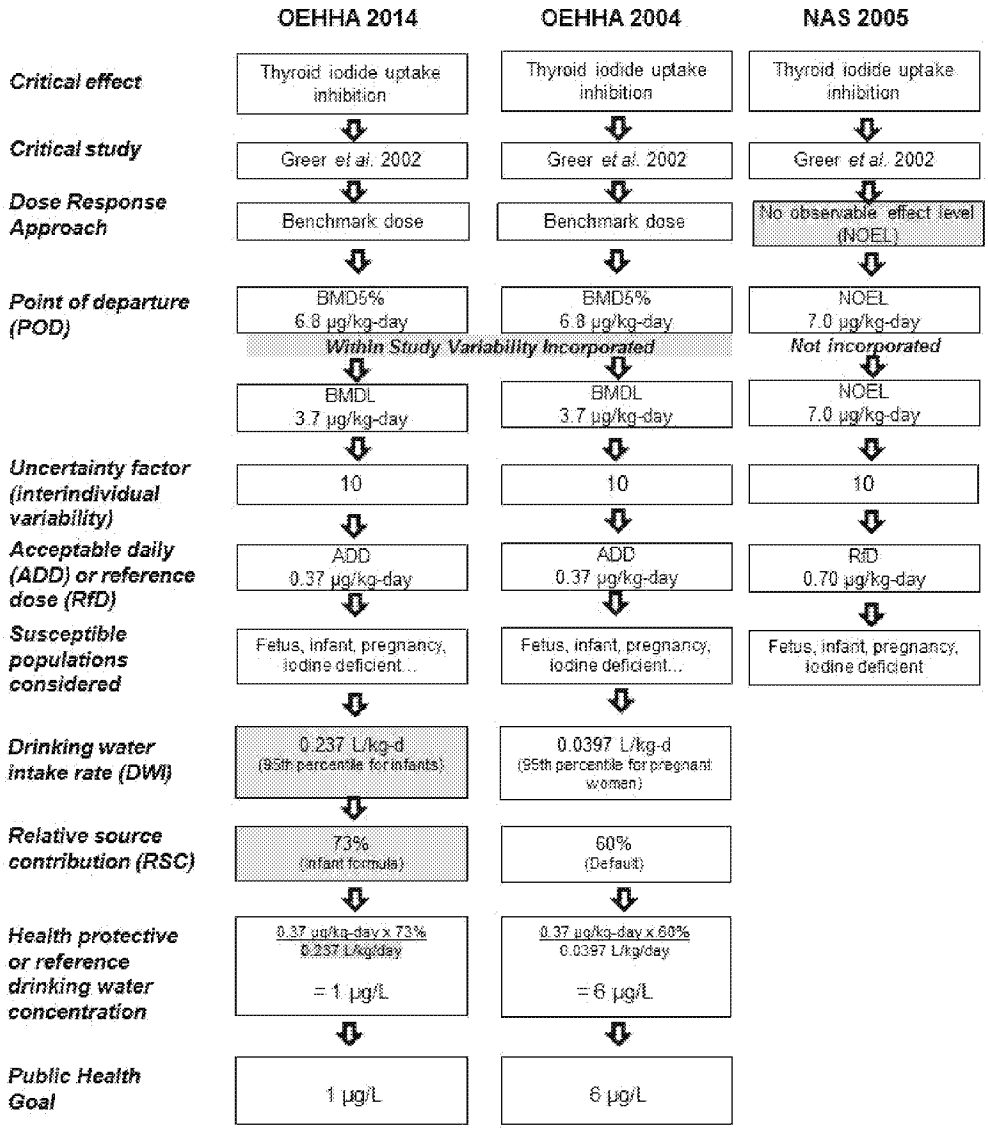
4. Both OEHHA and NAS identified the same populations likely to be more sensitive to perchlorate exposure: fetuses, preterm newborns, infants, developing children, pregnant women, people who have compromised thyroid function resulting from conditions that reduce thyroid hormone production, and people who are iodine-deficient.

There is only one substantive difference between the OEHHA and NAS analyses. The NAS used the no-observed-effect level (NOEL) approach. They determined that the NOEL was 0.007 mg/kg-day, the highest dose in the Greer *et al*. (2002) study that was not associated with a statistically significant response. OEHHA used the Benchmark Dose (BMD) approach and calculated a point of departure of 0.0037 mg/kg-day. As discussed above, the BMD method is a statistical method that is now widely recognized as a better approach because it incorporates more dose-response information from the study than the NOEL method (NAS, 2009; U.S. EPA, 2012).

From the NOEL, the NAS calculated a reference dose of 0.0007 mg/kg-day (the NOEL divided by the uncertainty factor of 10). OEHHA similarly calculated an ADD of 0.00037 mg/kg-day (the BMD-derived point of departure divided by the same10-fold uncertainty factor). Thus the two approaches differ by less than a factor of 2. The NAS did not take the next step to calculate an acceptable drinking water level for perchlorate.

A comparison of the NAS methods to those of this PHG and OEHHA's 2004 perchlorate PHG are shown in Figure 13.

Figure 13. Comparison of the Methods Used to Calculate OEHHA's Current and 2004 Perchlorate PHGs with the Methods Used by NAS (2005)



Conclusion

The primary toxic mechanism of perchlorate is a reduction in iodide uptake into the thyroid gland. If severe enough, this can lead to reduced thyroid hormone production. Adequate supplies of thyroid hormone are vital for a variety of physiologic processes, and even small reductions in thyroid hormone have been associated with increased cardiovascular disease risk factors, abnormal fetal brain development, and altered childhood cognition. The purpose of this updated PHG of 1 ppb is to identify a level of perchlorate in drinking water that prevents perchlorate-related reductions in thyroidal iodide uptake and subsequent decreases in thyroid hormone production that may be associated with any of these adverse health effects.

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APPENDIX 1: ALTERNATIVE BENCHMARK DOSE CALCULATIONS USING BLOUNT *ET AL.*, 2006 DATA

Study Description

Blount *et al.* (2006) was a cross-sectional study of urinary perchlorate levels and serum levels of thyroid hormones in 2,299 men and women ≥ age 12 who took part in the 2001-2002 National Health and Nutrition Examination Survey (NHANES). NHANES was conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention (CDC) and was designed to assess the health and nutrition status of the non-institutionalized population of the U.S. This survey involved a complex multistage sampling design with some over-sampling in certain areas and among certain subgroups, but was designed to provide results that are nationally representative. Information that was collected as part of this survey included questionnaire data on demographic information, smoking, health history, and medication use. A single serum measurement of T4 and TSH and a single measurement of urinary perchlorate and iodine concentration were also collected. Other information collected included urinary creatinine, thiocyanate, and nitrate; and serum levels of albumin, cotinine, and c-reactive protein.

The authors assessed the relationship between serum thyroid hormone levels and urine perchlorate concentrations using a linear regression analysis adjusted for potential confounding variables and co-variates including age, urinary creatinine, estrogen use, c-reactive protein, cotinine, ethnicity, menopause, premenarche, pregnancy, fasting time, body mass index, and kilocalorie intake. Several factors including urinary perchlorate and creatinine and serum TSH were logarithm transformed to normalize their distributions. Exclusions included subjects with missing data on co-variates, a history of thyroid disease, current use of thyroid medications, extreme values of T4 or TSH (n = 3), and subjects missing perchlorate measurements.

No association was found between T4 or TSH and perchlorate in men. In women, separate analyses were done for urinary iodine levels above and below 100 µg/L. This level was chosen since it is used by the World Health Organization to define iodine deficiency in a population. Thirty-seven percent of the women in this study had urinary iodine levels below 100 µg/L. The results of the analyses in women are shown in Table A1. A statistically significant association was seen between increasing TSH and increasing perchlorate in women with iodine levels above and below 100 µg/L. A statistically significant association was also seen between decreasing T4 and increasing perchlorate in women with urinary iodine levels below 100 µg/L but not in women with iodine levels above 100 µg/L.

Table A1. Associations between Thyroid Hormone Levels and the Logarithm of Urinary Perchlorate in Women with High and Low Levels of Urinary Iodine (Blount *et al.*, 2006)

	N	β	SE	p-value
Urine iodine < 100 µg/L				
T4	348	-0.8917	0.1811	<0.0001
Logarithm of TSH	356	0.1230	0.0373	0.0010
Urine iodine ≥ 100 µg/L				
T4	724	0.2203	0.3687	0.5503
Logarithm of TSH	697	0.1137	0.0506	0.0249

Abbreviations: β, regression coefficient; N, number of subjects, SE, standard error of the regression coefficient.
Differences in the numbers of subjects with an iodine category are due to differences in the number of subjects missing data on co-variates in each analysis. Except for perchlorate and creatinine, only co-variates with p-values < 0.10 were retained in each model.

Selection of the Key Biochemical Effect, Critical Study, Benchmark Response (BMR), and Control Group

Defining the Key Biochemical Effect

Thyroid hormone. As discussed in the previous sections, perchlorate has been associated with a variety of health and physiological effects. Focus is placed on perchlorate's impacts on the thyroid gland for the following reasons:

- These effects have been reported at lower exposure levels than the other significant health effects associated with perchlorate. By preventing low-dose thyroid effects, these other effects should also be prevented.
- Thyroid hormone is a very important hormone for homeostatic control in humans and alterations in thyroid hormone production have been associated with serious adverse outcomes, including diminished cognitive development and IQ in children and increased cardiovascular disease risk factors in adults.
- As discussed below, detailed dose-response data on perchlorate and thyroid hormone levels meeting the major tenets of causal inference are available from Blount *et al.*, 2006.

Is this adverse? While some people may not consider decreased T4 or increased TSH to be an "adverse" health outcome in isolation, as detailed in the PHG document, decreases in T4 are very closely associated with outcomes that are clearly adverse such as childhood cognitive development and alterations in lipid metabolism (which are closely linked to cardiovascular diseases).

Statistically significant dose-response relationships have been seen between T4 and each of these outcomes in studies which involve at least some subjects with T4 or TSH values at levels traditionally considered to be within normal reference ranges (discussed in previous sections).

Selecting the Critical Study

The data on women with urinary iodine levels below 100 µg/L evaluated in Blount *et al.* (2006) and collected as part of NHANES 2001-2 were used for the point of departure calculations. These data showed a clear, statistically significant dose-response relationship in a group of subjects that are an essentially representative sample of all subjects ages 12 years and older in the U.S. Because this is basically a representative sample, the levels of perchlorate exposure seen in this group are likely to be those commonly found in the general U.S. population. Other reasons for selecting this study include:

- Its relatively large sample size, which helps ensure adequate statistical power.
- Its inclusion of a relatively large number of people who are potentially susceptible to perchlorate (i.e., women with low iodine intake). Other clinical dosing or occupational studies did not specifically examine susceptible groups. Using these other studies could therefore underestimate effects in susceptible populations.
- It is a human rather than an animal study.
- The individual data are publicly available.
- The findings linking perchlorate to thyroid effects are consistent with the major tenets of causal inference (reviewed in earlier sections).

In the NHANES 2001-2 dataset, the association between T4 and perchlorate was particularly strong in women with both low iodine levels and high thiocyanate levels (Steinmaus *et al.*, 2007). OEHHA did not use the high thiocyanate group for our dose-response analysis since it involved only a relatively small number of subjects (n = 78).

Using raw data from NHANES: The main outcome variables in the Blount *et al.* (2006) study are serum levels of T4 and TSH. Levels of these hormones, as well as urinary levels of perchlorate and data on numerous potential co-variates are available for each individual in the study on the NHANES website. Since these data are publicly available OEHHA performed its own calculations using the individual data rather than relying on the grouped data and final results presented by Blount *et al.* (2006). As we have shown, the results of our analyses (Steinmaus *et al.*, 2007) are very similar to those of Blount *et al.* (2006). The minor differences are probably due to differences in the statistical packages used and differences in the way certain potential co-variates were defined. Performing

the calculations with the raw data allowed OEHHA to confirm the statistical analyses of Blount *et al*. (2006) and allowed a more thorough evaluation of specific aspects of causal inference (presented previously).

The Benchmark Dose Approach

The benchmark dose (BMD) approach was used to calculate a point of departure (POD). The advantages of this approach over the NOAEL approach are discussed elsewhere (U.S. EPA, 2000). The BMD is defined as the dose (or exposure) that causes a prescribed response rate (Crump, 2002). A statistical lower bound of the BMD, usually the 95% lower confidence limit (the BMDL), is used as the point of departure for defining an exposure level that is likely to be without an appreciable risk of deleterious effects in humans. Using the BMDL rather than the BMD helps to account for the uncertainty inherent in a given study and according to the U.S. EPA, "assures (with 95% confidence) that the desired response is not exceeded (U.S. EPA, 2000)." The BMD and BMDL are calculated by fitting a mathematical model to dose-response data and determining the dose, and its 95% CI, that is associated with a predefined benchmark response (BMR).

BMD for continuous data. In the past, the BMR has been typically defined as a 10 percent increase in the proportion of subjects exhibiting a predefined adverse response over the baseline response (the proportion exhibiting the response in a control or unexposed group). The 10 percent level is based primarily on the level of response that can be detected with sufficient statistical power in typical sized animal and human studies. Benchmark dose calculations can also be done for response data that are continuous. The 2004 OEHHA perchlorate PHG, which used a 5 percent decrease in radioactive iodide uptake, is an example of using a response variable that is continuous.

Selecting the BMR

Several approaches can be used to define a BMR:

An absolute level of T4 that is generally considered to be adverse: There is no single value of T4 or TSH that most clinicians would consider to define "adverse." Sometimes, the upper and lower 2.5th percentiles of T4 values collected in large population samples like NHANES have been used to define "normal" reference ranges. However, these levels are not absolute: some people with T4 levels outside these reference ranges will not exhibit thyroid disease, while some with T4 values within the normal reference range will. As discussed in the PHG document, several studies have shown linear associations between T4 and disease-related markers at T4 values well within normal reference ranges. For these reasons, there is no single absolute value of T4 which can be used to separate those likely to have significant risks of thyroid-related disease from those likely to have no risk of disease. Regardless, T4 percentile cut-off points are related to the risks of thyroid disease. That is, at least at the lower spectrum of T4 levels, the lower the percentile a subject's T4 value falls into, the greater

their risk of thyroid-related disease. Because of this, OEHHA evaluated the use of various percentiles of T4 in NHANES (the lower 2.5th, 5th, and 10th percentiles) as cutoff points for defining people likely to have a substantial risk of thyroid-related disease. This is discussed in further detail below.

Dichotomizing the data: One way of defining a BMR would be to dichotomize the outcome data; that is, define a serum level below which T4 would be considered adverse and above which it would not be considered adverse. As mentioned above, this could be defined as the lower 2.5th or 5th percentiles of T4 levels in a large population sample. Once dichotomized, the BMR can then be defined as an increase of 10 percent in the proportion of subjects that exhibit T4 levels below this cut-off point compared to the proportion seen in an unexposed (or relatively unexposed) control group. The problem with this approach is that much of the detailed information that is part of the continuous data set is lost, with a potential reduction in statistical power. The hybrid approach discussed below is one method for overcoming this problem.

Absolute or percentage change: Another approach for defining a BMR is to use a level of change in T4 that is generally considered to be biologically significant. For example, a 10 percent decrease in T4 from the mean T4 of an unexposed control group might be considered to be an important change. The BMD would then be the perchlorate dose associated with this 10 percent decline in T4. One problem with this method is that there is no single level of change in T4 that is universally accepted as being adverse or important.

Any change or any detectable change: Given the linear relationship between T4 and lipid metabolism and the linear relationship between T4 and childhood cognition that may occur within normal ranges of T4, it might be suggested that *any* decrease in T4 should be considered important. This is especially relevant on a population basis where any measurable decrease in population mean T4 would likely cause an increase in the number of people with T4 levels in the adverse range. For this reason, OEHHA evaluated the possibility of defining a BMR as a relatively small decrease in T4 (e.g., 1 percent and 5 percent) from the mean T4 in an unexposed control group. The problem with this method is that the selection of 1 percent or 5 percent could be considered arbitrary. In other words, one might ask why a 0.5 percent decrease or a 0.0001 percent decrease was not selected.

Because of this, OEHHA considered another approach: defining a BMR as any decrease in T4 that is detectable statistically. This is similar (albeit not the same) to the BMR approach used for outcome data that are dichotomous, where the BMR is typically defined as an increase of 10 percent in the proportion of subjects eliciting a predefined adverse effect. The value of 10 percent is used because it is the level of response that can be seen with sufficient statistical power in study designs and sample sizes commonly used in animal and human studies (U.S. EPA, 2000). Standard sample size calculations (Hulley and Cummings, 1988) and the variance in T4 seen in the 385 women with low iodine

in NHANES 2001-2 were used to estimate the change in T4 that is likely to be detectable with sufficient statistical power in this group of women. OEHHA's calculations suggest that a study this size would have 86 percent power to detect about a 10 percent decrease in mean T4 comparing a group the size of the lower 10^{th} percentile (i.e., 38 subjects) to the remaining subjects (i.e., 385 – 38 = 347 subjects). This power is close to the 80 percent level that most researchers would consider minimally adequate. The lower 10^{th} percentile was used in these calculations because subjects in the lower 10^{th} percentile of urine perchlorate were used as the "unexposed" control group in the BMD calculations (discussed below). Based on these statistical power estimates, a 10 percent decrease in mean T4 was selected as the BMR, although other levels of BMR were assessed for comparison purposes.

Selecting an Unexposed or Lesser Exposed Control Group

Since all of the subjects in NHANES 2001-2 had detectable levels of perchlorate, there is no truly unexposed group. Because of this, the following methods for defining a control group were considered:

a. *Lowest detected dose:* One method is to use the lowest dose detected as the baseline or control dose (0.19 µg/L). The problem with this method is that the control T4 level would be based on only one subject (only one of the 385 low iodine women had a urine perchlorate level of 0.19 µg/L) and therefore it would not be appropriately robust.

b. *Predicted T4 for the lowest detected dose:* Another method is to use the regression model to predict a mean T4 expected for a perchlorate dose of 0.19 µg/L. Since this T4 estimate is essentially based on the regression model (and all of the data that went into it), it would be more robust. The problem with this method is that the control group mean T4 would be based on a model prediction rather than on an actual set of real values.

c. *Predicted mean T4 for a perchlorate level of zero.* Another method would be to use the regression model and enter perchlorate as zero. The problem with this method is that the model includes the logarithm of perchlorate (log-perchlorate) and there is no logarithm of zero.

d. *A log-perchlorate of zero.* Another method could be to use the regression equation to estimate a mean T4 at a log-perchlorate of zero. The problem with this method is that a log-perchlorate of zero corresponds to a perchlorate level of 1 µg/L, and there is no obvious rationale for using a urinary concentration of 1 µg/L as the control level.

e. *Actual data.* The other option evaluated was using actual data from the low iodine women in NHANES 2001-2 and defining the control group as those subjects below a particular percentile cut-off point for perchlorate dose. Subjects with perchlorate values in the lower 5^{th}, 10^{th}, and 20^{th} percentiles of

creatinine-adjusted urinary perchlorate concentrations were used for this. It was decided to use a control group defined as those subjects in the lowest 10th percentile of creatinine-adjusted perchlorate residuals. This was chosen because: 1) the lower 10th percentile was the basis of the statistical power calculations used to define the BMR of 10 percent (described above); 2) it was necessary to categorize perchlorate into ten equal size dose groups in order to use these data in the BMDS (described below).

The Standard Deviation and Hybrid Approach

One standard deviation (SD): The U.S. EPA suggests in the absence of any other idea about what level of response to consider adverse, a change in the mean of the outcome (T4) equal to one standard deviation from the control mean can be used (U.S. EPA, 2000). They also recommend that regardless of what approach is used, the standard deviation approach be presented for comparison. Crump and others have shown that for a response variable that is normally distributed, a decrease of one SD corresponds to an increase of about 10 percent in the proportion of subjects falling below the 2nd percentile value of an unexposed comparison group (Crump, 1995).

Hybrid approach: The hybrid approach uses the distribution of a continuous variable (i.e., a mean T4 and its standard deviation) to estimate the proportion of subjects falling below a predefined percentile cutoff point (Gaylor and Slikker, 1990; Crump, 1995). This is done by converting the mean T4 in the unexposed group and the BMR into units on the standard normal deviation scale.

Crump and others present a method for determining the fraction of the standard deviation of the mean outcome value (i.e., T4) that corresponds to a particular proportion of subjects that fall below (or above) a particular percentile cutoff point. For example, if a T4 value below the 2.5th percentile in an unexposed control population is considered adverse, then a decrease in T4 corresponding to 0.82 times the T4 standard deviation corresponds to a BMR of 10 percent (i.e., a 10 percent increase in the proportion of people that will fall below the 2.5th percentile cut-off point). The equation is:

$$BMR = Q \times SD, \text{ where}$$

$$Q = N^{-1}[1-P(0)] - N^{-1}[1-P(0) - BMR]$$

N^{-1} is the inverse of the standard normal distribution (i.e., the z-score for the probability of 1-P(0) or 1-P(0)-BMR), and P(0) = the percentile below which is considered adverse (e.g., P(0) = 0.025 if being below the 2.5th percentile is considered adverse).

The Hybrid Approach Calculations

Standard deviations: The standard deviation in T4 for the 385 low iodine women in NHANES 2001-2 in the lower 5th, 10th, and 20th percentiles of creatinine-

adjusted perchlorate residuals were 1.87, 1.86, and 1.72, respectively. The similarity of these numbers shows that the variance in T4 is essentially independent of perchlorate dose.

Calculating Q. Values of Q were calculated for several levels of P(0) and BMR. Values for P(0) corresponding to the lower 2.5th and 5th percentiles of T4 were used since these have traditionally been used to define the lower bounds of "normal" T4 reference ranges. A P(0) value corresponding to the lower 10th percentile was also evaluated since significant cognitive effects were seen in children in the lowest 10th percentile of T4 or fT4 (Pop *et al.*, 1999, 2003: Kooistra *et al.*, 2006). BMRs of 5 and 10 percent were chosen since 5 and 10 percent are thought to represent levels that can be detected statistically in typical sized animal and human studies (U.S. EPA, 2000). Values of Q for these levels of BMR and P(0) are shown in Table A2.

Table A2. Hybrid Table: Calculating Values of Q

T4 considered adverse	P(0)	1-P(0)	N_A^{-1}	BMR	1-P(0)-BMR	N_B^{-1}	Q
< 2.5th percentile	0.025	0.98	1.960	5%	0.93	1.440	0.52
	0.025	0.98	1.960	10%	0.88	1.150	0.81
< 5th percentile	0.05	0.95	1.645	5%	0.90	1.282	0.36
	0.05	0.95	1.645	10%	0.85	1.036	0.61
< 10th percentile	0.1	0.90	1.282	5%	0.85	1.036	0.25
	0.1	0.90	1.282	10%	0.80	0.842	0.44

Abbreviations: BMR, the benchmark response or the increase in the proportion of people who fall below the T4 level considered adverse; N_A^{-1}, standard normal deviate for 1-P(0); N_B^{-1}, standard normal deviate for 1-P(0)-BMR; P(O), the percentile of T4 in the control group below which would be considered adverse.

Benchmark Dose Calculations

Transforming NHANES 2001-2 Data for the BMDS

The U.S. EPA BMD software (BenchMark Dose Software (BMDS) version 2.0) was used for the POD calculations. The following data transformations were required:

Creatinine adjustment: The BMDS does not allow the use of co-variates such as urine creatinine concentration. As shown above, urine creatinine was the only individual co-variate that caused a greater than 10 percent change in the perchlorate-T4 regression coefficient (Table 39). Because the addition of urinary creatinine appears to improve the model, it was decided that this variable should be incorporated into the POD calculations. This was done by calculating creatinine-adjusted perchlorate residuals ("perchlorate residuals") using the Proc

Reg statement in SAS with the logarithm of urinary perchlorate concentration (log-perchlorate) as the dependent variable and the logarithm of urinary creatinine concentration as the independent variable (logarithm of creatinine or log-creatinine). The association between serum T4 and the creatinine-adjusted perchlorate residuals was only slightly different than the association seen in the fully adjusted model.

OEHHA considered using the urine perchlorate:creatinine ratio. However, the association between T4 and this ratio in the low iodine women was not as strong as when perchlorate residuals were used and was only borderline statistically significant (unadjusted regression coefficient between T4 and the perchlorate:creatinine ratio = -1.18; SE = 0.66; p = 0.07). This is likely due to the factors discussed previously for the iodine/creatinine ratio. That is, it creates a variable that is not only dependent on perchlorate, but also on all the factors that determine an individual's urinary creatinine level (e.g., muscle mass, diet, physical activity, and many other factors). Including all these other influences into the perchlorate exposure variable can lead to misclassification of true perchlorate exposure.

Other co-variates and potential modifying factors: None of the other co-variates used in Blount *et al.* (2006) caused important changes in the perchlorate-T4 regression coefficient so these were not used in the BMD calculations. In addition, the NHANES complex sampling weights were not used because they had only a small impact on regression coefficients and their standard errors (Table A3), and the incorporation of these weights would have significantly complicated the model.

Table A3. T4-Log-Perchlorate Regression Coefficients Using Different Methods of Analysis

Method	Adjusted	Weights[a]	β	SE	p
Blount *et al.*, 2006	Full	Yes	-0.89	0.18	<0.0001
Steinmaus *et al.*, 2007	Full[b]	Yes	-0.73	0.22	0.004
	Full[b]	No	-0.87	0.27	0.0016
	Creatinine Only	No	-0.81	0.27	0.0026
	Unadjusted	No	-0.67	0.23	0.0041
BMDS	Creatinine Only	No	-0.79	0.28	na[c]

Abbreviations: BMDS, benchmark dose software; β, regression coefficient; SE, standard error; na, not available.
[a]NHANES sampling weights applied
[b]Only independent variables with p-values < 0.20 were entered and retained in the model except for log-creatinine which was retained in the model regardless.
[c]p-value not given. The 95% CI of the regression coefficient is -1.34 to -0.24

Figure A1 shows the linear relationship between serum T4 and the creatinine-adjusted perchlorate residuals. The effects of possible outlying values were assessed by removing certain data points. Removing the leftmost point in this figure (T4 = 10.1 µg/dL, urine perchlorate = 0.24 µg/L, urinary creatinine = 146 mg/dL) changed the regression coefficient from 0.8122 to 0.7924. Removing the rightmost data point in this figure (T4 = 7 µg/dL, perchlorate = 100 µg/L, creatinine = 40 mg/dL) changed the regression coefficient from 0.8122 to 0.8135.

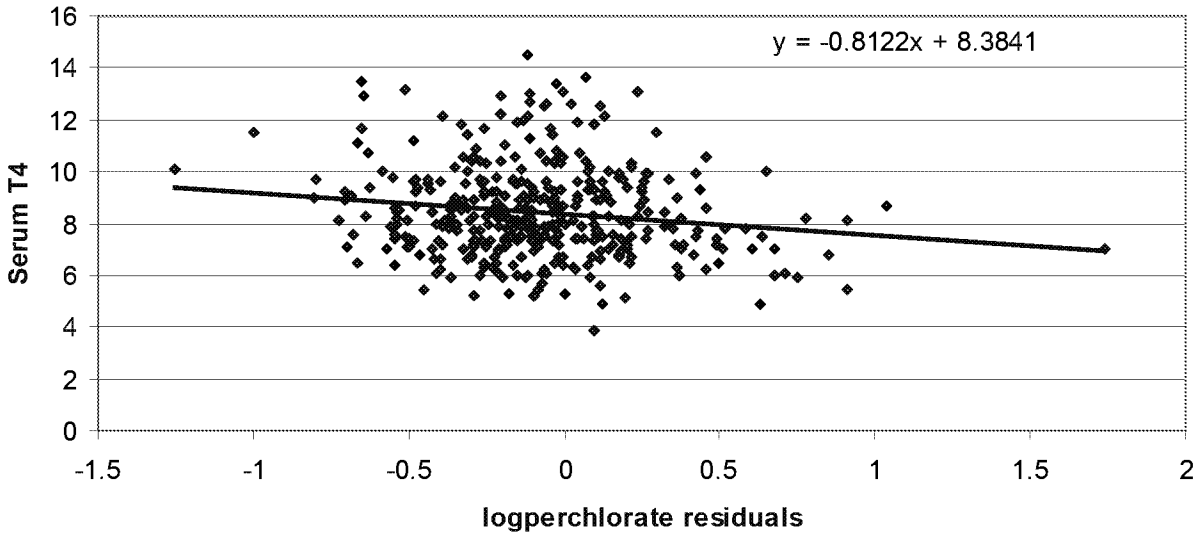

Figure A1. Serum T4 and Creatinine-adjusted Perchlorate Residuals in 385 Women with Urinary Iodine Levels < 100 µg/L, NHANES 2001-2

Categorizing dose: The BMDS allows for the use of individual data on dose and response and both can be entered as continuous variables. In controlled human trials, such as the Greer *et al*. (2002) study, doses are usually categorized into a relatively small number of dose groups. In NHANES 2001-2, each individual subject had their own urinary perchlorate concentration. Since there were 385 subjects in this study, this resulted in hundreds of "dose groups." Entering this many dose groups into the BMDS led to implausibly wide confidence intervals around the BMD and implausibly low BMDL values. To make the calculations computationally easier, perchlorate residuals were ranked into 10 equal sized dose groups and each individual in each group was assigned the mean perchlorate residual value for that group. Categorizing data into groups such as these can potentially cause a loss of information and decrease study power but this did not seem to be the case here. Table A4 compares the perchlorate-T4 model parameters calculated in SAS Proc Reg using the individual data versus those calculated by the BMDS using the 10 dose groups. As seen, the regression coefficient and its standard error are essentially the same in both models. This shows that using the 10 dose groups instead of the 385 individual dose points resulted in little loss in statistical power and essentially no loss in our ability to accurately measure the dose-response relationship.

Since the choice of using 10 dose groups was somewhat arbitrary, the effect of using more or fewer dose groups was evaluated. Table A4 shows the results of the BMDS calculations using 5 or 20 equal size dose groups. As seen, when five dose groups were used it appears that too much information was lost and the dose-response relationship becomes less strong. Using 20 dose groups didn't substantially change the model compared to when 10 groups were used.

Table A4. Association between T4 and Perchlorate Residuals: Comparing Individual Data to Dose Groups

Method	Intercept (SE)	β (SE)
SAS Proc Reg: individual data	8.04 (0.56)	-0.81 (0.27)
BMDS linear model:		
10 dose groups	8.88 (0.17)	-0.79 (0.28)
5 dose groups	8.68 (0.16)	-0.54 (0.30)
20 dose groups	8.99 (0.20)	-0.83 (0.27)

Abbreviations: β, regression coefficient; SE, standard error

Positive numbers for dose: The BMDS does not accept negative values for dose. The dose metric was perchlorate residuals, which had a mean of zero and some positive and some negative values. To prevent having any negative values for dose, the mean of the lowest dose group was subtracted from the means of each dose group to obtain a new dose variable for each group. This resulted in a value of zero for the lowest dose group and positive values of dose for all other groups. Since this maintained the absolute difference between doses it did not affect the perchlorate-T4 residual slope or its standard error.

Following these transformations, BMDS was used to calculate a BMD and BMDL. The BMD and BMDL are the creatinine-adjusted logarithm of urine perchlorate residuals minus the perchlorate residuals in the lowest dose group. These numbers were converted back into a urinary perchlorate level in µg/L using the following steps:

1. Adding the mean perchlorate residual in the lowest dose group (note that this is actually a negative number so adding it is the same as subtracting its absolute value). This gives the creatinine-adjusted residuals of the logarithm of urine perchlorate concentration.

2. Because the residuals have a mean of zero, and some positive and some negative values, they have no practical meaning in terms of an actual perchlorate concentration. To convert the residuals back to an actual value of log perchlorate, the log-perchlorate concentration that was predicted for the mean log-creatinine level of the study population as a whole was added using the method recommended in Willett and Stampfer, (1998). The predicted log-perchlorate concentration was calculated using SAS Proc Reg with log-perchlorate as the dependent variable and log-creatinine as the independent variable (the same equation used to calculate the residuals).

3. This number was then converted to a urine perchlorate level in µg/L by taking the inverse log.

Using the BMDS

The linear model using the continuous data option was selected in the BMDS. The individual data for serum T4 was entered as the response variable and the mean values for each dose group (as described above) were entered as the dose variable. As discussed above, subjects in the lowest 10^{th} percentile of perchlorate residuals were used as the "unexposed" control group and had a transformed dose value of zero. The BMR was set at a relative decrease in T4 of 10 percent. Other options selected were: the constant variance and BMD calculation boxes were checked. Parameter assignments were all set at "default," the degree of polynomial was set at 1, the confidence level was set at 95%, and the adverse direction was set at "down."

BMDS Results

The following table shows the BMD and BMDL calculations where the BMR is defined as a 10 percent decrease in T4 from the mean T4 in the "unexposed" control group. For comparison purposes, BMD calculations are also shown for other definitions of BMR:

- The hybrid approach was used, with Q values corresponding to a 5 percent (Q = 0.25) or 10 percent (Q = 0.44) increase in the proportion of subjects below the lower 10^{th} percentile of T4 in the "unexposed" control group. The lower 10^{th} percentile was chosen because this was the cut-off used to define the "low" fT4 group in Kooistra *et al.* (2006), Pop *et al.* (1999), and Pop *et al.* (2003), three studies that found statistically significant associations between low maternal gestational fT4 and childhood cognitive deficits.

- Calculations are shown for BMRs defined as 20-30 percent decreases in T4 because this was the level of difference in T4 and fT4 associated with statistically significant declines in child cognitive development in other studies.

- Calculations for a BMR equal to a one standard deviation change in the mean T4 of the control group are shown because U.S. EPA recommends that these always be shown for comparison purposes.

Table A5. BMD and BMDL Results for Various Levels of BMR

BMR	1%	5%	10%	20%	30%	0.25SD[a]	0.44SD[a]	1SD
BMD (from the BMDS)	0.11	0.56	1.13	2.26	3.38	0.56	0.98	2.23
BMDL (from the BMDS)	0.07	0.37	0.73	1.46	2.19	0.35	0.62	1.40
Step 1: Add the lowest dose								
Lowest dose	-0.544	-0.544	-0.544	-0.544	-0.544	-0.544	-0.544	-0.544
BMDL log-perchlorate residual	-0.471	-0.179	0.186	0.916	1.647	-0.194	0.072	0.857
Step 2: Convert residual to log-perchlorate								
log-perc at mean log-creat	0.251	0.251	0.251	0.251	0.251	0.251	0.251	0.251
Add mean log-perc to residual log-perchlorate	-0.220	0.072	0.437	1.167	1.898	0.057	0.323	1.108
Step 3: Take inverse log								
BMDL in µg/L (urine)	0.60	1.18	2.73	14.69	78.99	1.14	2.11	12.83
Convert urine µg/L to intake								
Age[b]	35	35	35	35	35	35	35	35
Weight[b]	66.7	66.7	66.7	66.7	66.7	66.7	66.7	66.7
Height[b]	160.9	160.9	160.9	160.9	160.9	160.9	160.9	160.9
k (constant, for females)	1.64	1.64	1.64	1.64	1.64	1.64	1.64	1.64
Gram creatinine/day estimate	1.190	1.190	1.190	1.190	1.190	1.190	1.190	1.190
Creatinine g/L[b]	0.53	0.53	0.53	0.53	0.53	0.53	0.53	0.53
Intake at BMDL (in µg/day)	1.4	2.6	6.1	33.0	177.3	2.6	4.7	28.8
Intake at BMDL (in µg/kg-day)	0.020	0.040	0.092	0.495	2.659	0.038	0.071	0.432

[a]The T4 standard deviation (SD) in the control group was 1.87 so 0.25SD = 0.4675 and 0.44SD = 0.8228.
[b]The median levels in all 385 low iodine women in NHANES 2001-2 were used for these values.

Converting urinary perchlorate concentrations to levels of perchlorate intake

In all of these POD calculations perchlorate dose is expressed in terms of a urinary concentration of perchlorate. These values were used to calculate the BMD and BMDL. These were converted into an estimated daily intake of perchlorate using the method presented in Blount *et al.*, 2007. This method is based on equations from Crockcroft and Gault (1976) and modified by Mage *et al.* (2004) and estimates perchlorate intake using urinary perchlorate and creatinine concentrations combined with estimates of daily creatinine output which are based on age, height, gender, and weight. This equation is:

$$\text{Daily perchlorate intake} = \frac{\frac{\mu g \text{ urine perchlorate}}{\text{gram urine creatinine}} \times \frac{\text{gm creatinine}}{\text{Day}}}{\text{kg}}$$

Where gm creatinine / day is estimated by:

$10^{-6} \times k \times (140 - \text{age(year)}) \times \text{weight(kg)}^{1.5} \times \text{height(cm)}^{0.5}$

Where k = 1.64 for females. The median values in the 385 low iodine women were used for age (35), height (160.9 cm), weight (66.7 kg), and urine creatinine concentration (53 mg/dL). The results of these calculations are shown at the bottom of Table A5.

Summary

OEHHA calculated an intake BMDL of 0.092 µg/kg-day for a 10 percent decrease in T4. This BMDL is reasonably close to that calculated using the hybrid approach corresponding to an increase of 10 percent in the proportion of subjects with T4 values below the lower 10^{th} percentile. The BMDS graphical displays of both of these analyses are shown in Figures A2 and A3.

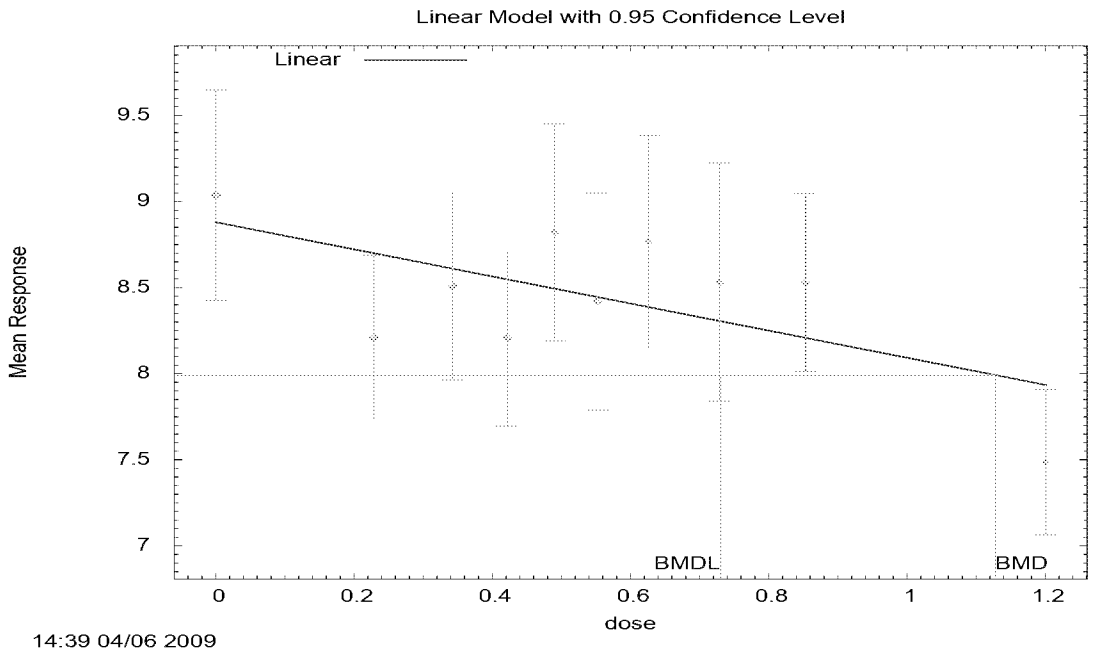

Figure A2. BMDS Output for Serum T4 (Mean Response) and Transformed Log Perchlorate Residuals (Dose) for a BMR of 10 Percent Decrease in T4

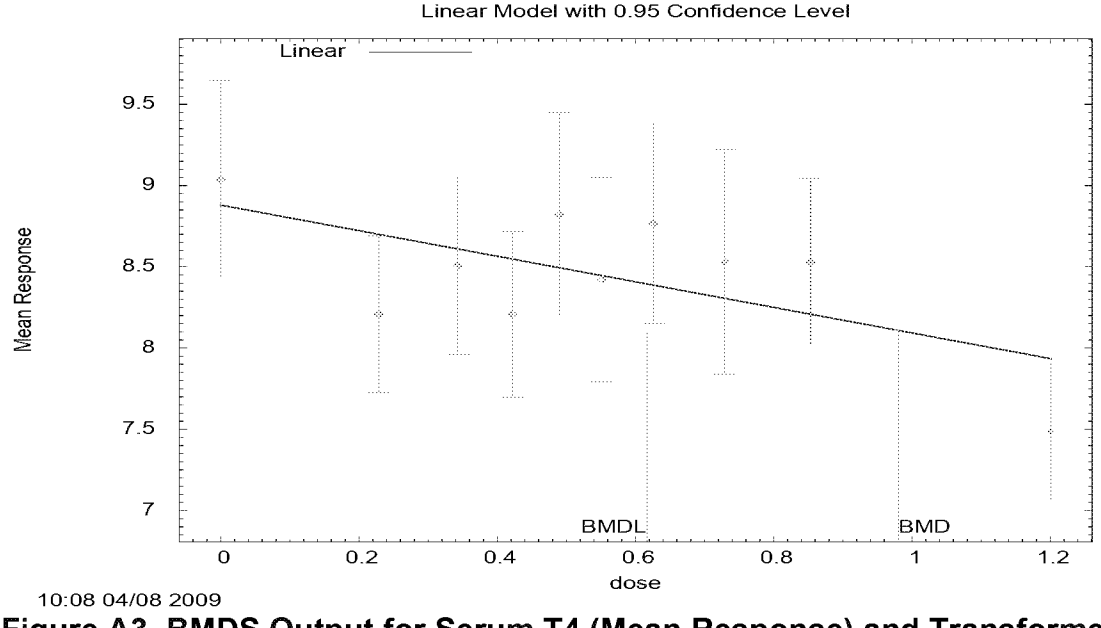

Figure A3. BMDS Output for Serum T4 (Mean Response) and Transformed Log Perchlorate Residuals (Dose) for a BMR of 0.44 x the T4 Standard Deviation of the Control Group

Calculation of the PHG Using NHANES 2001-2002 Data

Acceptable Daily Dose

For estimation of a health-protective concentration of perchlorate in drinking water, an acceptable daily dose (ADD) of the chemical from all sources will first be calculated. This involves incorporation of appropriate estimates of uncertainty in the extrapolation of the dose leading to the key biochemical effect from human or animal studies to the estimation of a lifetime ADD that is unlikely to result in or lead to any toxic effects. For this purpose, the following equation can be used:

$$\text{ADD} = \frac{\text{NOAEL/LOAEL/BMDL in mg/kg-day}}{\text{UF}}$$

where,

ADD = estimated maximum daily dose that can be consumed by humans for an entire lifetime without toxic effects;

NOAEL/LOAEL/BMDL = no-observed-adverse-effect level, lowest-observed-adverse-effect level, or lower limit on the benchmark dose estimated from the critical study;

UF = uncertainty factor(s).

For this case, the ADD is estimated from the lower limit of the two-sided 95 percent confidence interval of the perchlorate dose estimated to cause a 10 percent reduction in serum T4 levels, as observed in Blount *et al.* (2006). In this study, statistically significant associations between increasing perchlorate and decreasing T4 were seen in women with urinary iodine levels below 100 µg/L but not in women with higher iodine levels.

An uncertainty factor of four is used, including a factor of 2 to account for uncertainty due to the use of cross-sectional data to derive the dose-response estimates, and a factor of 2 to account for uncertainty due to possible increased susceptibility related to factors that were not already taken into account (e.g., exposure to other thyroid-inhibiting agents like thiocyanate, thyroid diseases, additional susceptibility in the fetus and young children). Thus,

$$\text{ADD} = \frac{0.092\ \mu\text{g/kg-day}}{2 \times 2} = 0.023\ \mu\text{g/kg-day}$$

Public Health Protective Concentration

Calculation of a public health protective concentration (C, in mg/L) for perchlorate in drinking water uses the following equation for noncarcinogenic endpoints:

C = ADD µg/kg-day × (BW/WC) × RSC

C = 0.023 µg/kg-day x 23.3 kg-day/L x 1

C = 0.54 µg/L = 0.5 µg/L (ppb) (rounded)

where:

(BW/WC) = the ratio of body weight (kg) and tap water consumption rate (L/day); the ratio for the 95th percentile of the pregnant woman population is estimated to be 0.0233 kg-day/mL or 23.3 kg-day/L (OEHHA, 2012 and Table 47 above); and

RSC = relative source contribution; a value of 1 is used for pregnant women. See the explanation for this value below.

Uncertainty factors

Susceptibility: Potential susceptible subpopulations were listed previously. It is likely that much of the susceptibility due to inadequate iodine intakes is already incorporated by using data on women with low iodine levels for these BMD calculations. In addition, some of the susceptibility due to several of the other factors listed above is likely already included in these calculations since NHANES is a population based study and involves at least some subjects who fall into the susceptible subgroups listed above. Because of this, OEHHA did not use the uncertainty factor of 10 that would typically be applied to account for inter-individual variability when dose-response data are derived from healthy individuals. However, some potentially susceptible groups were not included or were not specifically evaluated in the NHANES data set used. These include fetuses, infants and young children, people with thyroid diseases, and subjects exposed to high levels of other NIS inhibitors. An uncertainty factor was added to account for the potential susceptibility in these groups. Data from Steinmaus *et al.* (2007) suggest that the magnitude by which perchlorate reduces T4 levels is about 2 times greater in people with high thiocyanate levels than in people with average or low thiocyanate levels. Based on these findings an uncertainty factor of 2 was added, although it should be noted that the kinetics in rodents may be different than in humans, particularly with respect to the maternal-fetal transfer of chemicals.

Database weaknesses: An uncertainty factor was also added to account for the fact that this dose-response assessment is based on cross-sectional data. As discussed above, the single measurements of serum T4 and urinary perchlorate that were collected in NHANES 2001-2 may not be completely accurate measures of true long-term T4 levels or perchlorate exposure. Because this bias is most likely to be non-differential, the resulting impact on the perchlorate-T4 regression coefficient is likely to be towards a regression coefficient of zero, and true associations might actually be stronger than the one observed. Beaton *et al.* (1979) published an equation for predicting the magnitude of this bias:

$\beta_t = \beta_0 (1 + R^2_x/n_x)$,

where β_t is the estimated true regression coefficient after correcting for misclassification, β_0 is the observed regression coefficient, R^2_X is the ratio of intra- to inter-individual variances for the misclassified variable x, and n_x is the number of replicate measures of x per subject that were collected in the study. Since only a single urine and serum sample were collected from each subject in NHANES, $n_x = 1$, and the degree of bias is primarily related to R^2_x. Information on the value of R^2_x is not available in the NHANES 2001-2 data set, and OEHHA could not find a similar published study that specifically provided values of R^2_x for urinary perchlorate concentrations in humans.

In one study however, Ohira *et al.* (2008) compared 24-hour urine perchlorate measurements to creatinine-adjusted spot urine perchlorate concentrations in 14 breastfeeding mothers and reported that the average deviation between these two measures was 105 percent. In this NHANES study group, the mean spot urine perchlorate concentration was 2.86 µg/L. If one assumes the average deviation in the NHANES population was similar to that of Ohira *et al.* (2008), then the average deviation between a single spot urine perchlorate concentration and 24-hour sample concentrations in the NHANES study group would be about 3.0 µg/L (i.e., 105 percent x 2.86 µg/L).

Assume that:

1. The *mean* perchlorate concentration in spot samples from a large group of subjects (x_m) will be about equal to the *mean* perchlorate concentration in 24-hour samples from this same large group (this is probably a valid assumption because while a spot concentration may vary from a 24-hour concentration in any given individual, the spot concentration and 24-hr concentration means in the group should be about the same), and

2. The mean perchlorate concentration in 24-hour samples is a much better reflection of true perchlorate intake than perchlorate concentration from a spot urine sample (more on this later).

Then an estimate of the variance due to intra-individual variability associated with the use of spot samples might be estimated as:

Variance = $\sum (x_m - x_i)^2 / n - 1$,

where n is the number of subjects in the study, and $x_m - x_i$ is the average deviation between spot urine and 24-hour urine concentrations (3.0 µg/L). Given

this, the estimate of intra-individual variance is:

$$= 385 * (3.0\ \mu g/L)^2 / (385-1)$$

$$\approx 9\ \mu g/L$$

The total variance (intra- and inter-individual variance) in the spot urine perchlorate concentrations in the NHANES 2001-2 data set (all 385 low iodine women) was 32.9 µg/L. These data suggest that R^2_x might be somewhere near:

R^2_x = variance $_{\text{intra-individual}}$/variance $_{\text{inter-individual}}$

$$= 9\ \mu g/L / (32.9\ \mu g/L - 9\ \mu g/L) = 0.38$$

The corrected regression coefficient could be somewhere near:

$$\beta_t = \beta_0 (1 + R^2_x/n_x)$$

$$= 0.79 (1 + 0.38/1) = 1.09$$

That is, the corrected regression coefficient between perchlorate and T4 is about 1.09 times larger than the observed coefficient.

It should be noted that these calculations are estimates. They are based on the assumptions that 24-hour perchlorate levels are an accurate indicator of true long-term exposure and that the variance in the NHANES population is similar to that of Ohira *et al*. (2008). In addition, they do not take into account other sources of variance like laboratory imprecision. Despite this, these estimates do provide some general idea of the likely magnitude of the bias due to the use of spot urine samples and provide at least some assurance that a factor of two is likely to cover the uncertainty associated with this database insufficiency.

With regards to intra-individual variability in serum T4 measurements, Andersen *et al*. (2001) examined this issue in 16 healthy men by collecting monthly measurements of serum T4 over a period of one year. They reported an individuality index (defined as $SD_{\text{analytical+intraindividual}} / SD_{\text{interindividual}}$) of 0.54. A ratio of the respective variances (i.e., R^2_x) would be about $(0.54)^2 = 0.29$. This possible 29 percent increase in the perchlorate-T4 regression coefficient is also within the two-fold uncertainty factor that was incorporated.

Relative source contribution

Recent food analyses have greatly expanded the data available on exposures to perchlorate in food, as described in the Exposure section of this document. Perchlorate has been detected in a wide variety of foods, including fruits, vegetables, grains, dairy milk, and human breast milk (Kirk *et al*. 2005, Pearce *et al*., 2007; Murray *et al*., 2008). Perchlorate levels in urine from NHANES, as reflected in the analysis of Blount *et al*. (2006), are generally supportive of the

FDA analysis. Together, these data demonstrate that food is the primary source of perchlorate for the general population.

At an ADD of 0.023 µg/kg-day and a range of average perchlorate exposure levels in food of about 0.09 to 0.39 µg/kg-day, the health-protective level is already exceeded by perchlorate from food. Mean exposures from food for women of childbearing age are about 0.1 µg/kg-day, according to the estimates of Murray *et al.* (2008). Thus it does not seem appropriate to allocate any specific fraction of total exposure to drinking water; all sources should be limited because the threshold of effect is already exceeded by the exposures derived from food. The concept of zero as a relative source contribution from water is unattainable. We have used 1 as a placeholder, indicating that no specific "acceptable" fraction can be calculated.

Drinking water at a PHG level of 0.6 ppb would provide about one/tenth the average exposure to perchlorate that would be obtained from food, for women of child-bearing age. One could say that this is equivalent to a relative source contribution of 0.1, which is below the guidelines of 0.2 to 0.8 recommended by U.S. EPA. However, these guidelines are intended for exposures that yield total daily doses below the effect threshold. In this case, since effects on thyroid hormone homeostasis are observed at common environmental exposures, the operating principle should merely be to decrease exposure to perchlorate as much as practical, and ensure adequate dietary iodine.

UPDATE TO "PERCHLORATE TOXICOLOGICAL PROFILE AND HEALTH ASSESSMENT"

In support of:
Perchlorate Maximum Contaminant Level (310 CMR 22.06)
Perchlorate Cleanup Standards (310 CMR 40.0000)

June, 2006

Office of Research and Standards
Massachusetts Department of Environmental Protection
1 Winter Street
Boston, Massachusetts USA

PREFACE

This document presents an update to MassDEP's 2004 *Draft Toxicological Profile and Health Assessment.* MassDEP postponed finalization of the 2004 document in order to consider the National Academy of Science's (NAS) report, *Health Implications of Perchlorate Ingestion,* which was released in January 2005, as well as additional information on perchlorate in breast milk that was not available to the NAS Committee. A separate MassDEP document, released concurrently with this document, titled *Addendum: Review of New Studies on Perchlorate*, addresses results from several even more recent scientific studies that were published during the internal review period for this updated document. This document reflects the scientific review and deliberation of MassDEP scientists, as well as distinguished members of the MADEP/DPH Advisory Committee on Health Effects. Two local members of the NAS committee met with MassDEP and its Advisory Committee to share information and perspectives on the health effects of perchlorate.

Table of Contents

List of Tables

List of Figures

PEER REVIEW: DEP/MA DPH ADVISORY COMMITTEE ON HEALTH EFFECTS

MassDEP employed its standing advisory committee on health effects to advise it during the preparation of this document. The Committee membership was augmented with a number of specialists with expertise in the subject areas covered in our assessment of the health effects of perchlorate and standard setting. Participants included:

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ACKNOWLEDGEMENT

MassDEP is very appreciative of the participation of the members of the MassDEP/DPH Advisory Committee on Health Effects in the scientific peer review of MassDEP's draft updated toxicity assessment. Their generous commitment of time and tremendous expertise has been extremely helpful to our efforts on this important issue. The participation of independent public health scientists is a critical component of our state's efforts to protect public health and the environment in MA.

MassDEP also wishes to acknowledge two members of the National Academy of Sciences' Committee to Assess the Health Implications of Perchlorate Ingestion, Dr. Robert Utiger (Harvard University School of Medicine, Boston, MA) and Dr. Rosalind Brown (Children's Hospital, Boston, MA) for sharing information and perspectives on the toxicity of perchlorate with MassDEP and the Advisory Committee during the February 11, 2005 meeting. MassDEP is also grateful for the valuable input and information provided by Charles Emerson, MD, endocrinologist, University of Massachusetts Medical Center, Worcerster, MA.

EXECUTIVE SUMMARY

The following document provides an update of the Massachusetts Department of Environmental Protection's (MassDEP) 2004 *Draft Toxicological Profile and Health Assessment*, taking the National Academy of Sciences (NAS) report on perchlorate released in January 2005 into account, as well as other recent data.

Perchlorate inhibits iodide transport into the thyroid gland, which is hypothesized to be its primary mechanism of toxicity. The thyroid requires iodide to make thyroid hormones, which are essential for the normal growth and development of many systems in the body including the brain (MassDEP, 2004; U.S. Environmental Protection Agency, 2002a). Perchlorate is itself concentrated into breast milk in experimental animals and likely in humans as well; it may also be concentrated into thyroid cells, where it could impact other cellular functions. It may also interfere with iodide transport into breast milk, and interfere with a second iodide transporter found in the thyroid. Although not well understood, perchlorate also promotes the discharge of accumulated iodide from the thyroid gland at high doses. These effects of perchlorate, whether working in concert or independently, may, at sufficient doses, disrupt normal thyroid function and hormone dynamics, including altered synthesis of essential thyroid hormones (thyroxin (T4) and triiodothyronine (T3)).

Based on many lines of evidence premature infants and newborns are particularly at risk from perchlorate toxicity. Their sensitivity is attributable to the development of various organs, especially the brain, which occurs during fetal growth and early childhood. Appropriate levels of thyroid hormones are critical to these processes.

During the fetal and newborn periods the thyroid gland is also incompletely developed, increasing sensitivity to toxicants that disrupt the thyroid functions available. Pregnancy itself stresses maternal thyroid function increasing risks to the fetus. To further compound matters, breast milk is the sole source of the iodide a newborn needs to supply its capacity to synthesize thyroid hormones. Data suggests that maternal exposure to perchlorate may reduce iodide levels in breast milk, and thereby may increase neonatal sensitivity to perchlorate. This risk is further compounded by the fact that perchlorate is itself secreted, and may be concentrated, into the milk, presenting a double insult to the newborn's thyroid (Kirk et al. 2005).

Despite their likely sensitivity, there is essentially no good toxicity data on perchlorate exposures to pregnant women, the fetus and newborn. Thus, regulators must extrapolate from controlled studies on small numbers of healthy adults and/or data from animal (rodent) model systems. The current epidemiological data on larger groups of people exposed to perchlorate does not allow for safe exposure levels to be determined.

The MassDEP *Draft Toxicological Profile and Health Assessment* was undertaken as the result of a public request for guidance on drinking water perchlorate contamination, as no federal or state standards on this toxicant were available. In the MassDEP 2004 *Draft Toxicological Profile and Health Assessment*, MassDEP used a weight of the evidence approach in which data from animal and human studies were both assessed. These were found to yield overlapping toxicity values. Because the animal studies included exposures to the fetus and newborn, the

lifestages most at risk, Mass DEP relied on data from that research to derive an acceptable total human dose or RfD of 3×10^{-5} mg/kg-day.

While MassDEP was working on its 2004 Assessment the National Academy of Sciences (NAS) convened a scientific advisory committee to address perchlorate toxicity. The NAS completed its report in January 2005, and derived two possible RfD values using data from the 14-day perchlorate exposure study performed on small groups of healthy adults by Greer, et al. (2002). The majority of the NAS Committee members supported an RfD of 7×10^{-4} mg/kg-day, treating the lowest dose given to a group of 7 healthy adults in the Greer study as a no effect level and applying a total uncertainty factor of 10. One member of the NAS committee concluded that an additional uncertainty factor of 3, for a total uncertainty factor of 30, was needed to account for deficiencies in the database. Including this additional factor results in an RfD of 2.3×10^{-4} mg/kg-day.

The following document provides an update of MassDEP's *Draft Toxicological Profile and Health Assessment* taking the NAS report released in January 2005 into account, as well as even more recent data on perchlorate in breast milk and perchlorate in the U.S. food supply that was not available to the NAS Committee. In summary, MassDEP scientists in consultation with the MassDEP/DPH Advisory Committee on Health Effects concluded that a weight of the evidence approach should continue to be used to determine the most appropriate RfD value and corresponding drinking water limit. Thus, both the human and animal data were again considered. However, in part based on the NAS report, MassDEP is now placing more weight on the human data, which is used as the point of departure to derive MassDEP's current recommended RfD.

Upon consideration of the NAS report, MassDEP and the MassDEP/DPH Advisory Committee on Health Effects concurred with the NAS committee's view that the iodide uptake inhibition (IUI) data in the Greer et al. study constitute a reasonable basis for determining an RfD, provided that the inherent limitations and uncertainties in the data are appropriately accounted for. MassDEP believes the following factors must be addressed when using the Greer study to derive an RfD: protection of sensitive subgroups, since the Greer study involved adults; uncertainty in defining a true no adverse effect level, given the small number of subjects in the low dose group; and data gaps resulting from new information that became available after the NAS recommended an RfD.

Mass DEP is deriving an RfD for perchlorate by using the traditional approach and long-standing protocol also used for other chemicals. MassDEP supports the designation of iodide uptake inhibition (IUI) as a critical effect and point of departure (POD) for the development of an oral RfD for perchlorate. This position is consistent with U.S. EPA policy for setting RfDs (U.S. Environmental Protection Agency, 2002). The critical effect is defined as the first adverse effect, or its *known precursor*, that occurs to the most sensitive species, as the dose rate of the agent increases. We treat the lowest dose in the Greer study as a minimal Low Observed Adverse Effect Level (LOAEL), requiring application of an uncertainty factor of 3 to derive a No Observed Adverse Effect Level (NOAEL). MassDEP has concerns about the lowest dose in the Greer study being a no-effect level based on the facts that: due to the small number of subjects in the lowest dose group, there is low power to detect a statistically significant effect; averaging of

group responses obscures positive individual inhibition; a non-statistically significant IUI effect was observed at the lowest dose tested; and, good low dose corroborating data is lacking. Furthermore, we treat iodide uptake inhibition as an adverse effect, because to our knowledge, no human data exists that demonstrates the level of iodide uptake inhibition necessary to cause downstream effects, especially for the sensitive subgroups. At this time, the relationship between IUI and thyroid hormone synthesis, especially in the fetus and neonate, is unknown. Indeed the available data from studies on animals suggests that adverse effects may be associated with low levels of IUI. Thus, we treat IUI, which is an early event in the putative mechanistic pathway leading to perchlorate toxicity, as being causative of adverse effects and thus an effect to be avoided itself. Our use of this effect as a point of departure in deriving an RfD is consistent with US EPA policy for deriving RfDs.

MassDEP is also taking into account new information demonstrating perchlorate's widespread presence in breast milk in the US. Perchlorate was detected in 36 of 36 samples taken from a wide geographic area, at an average concentration of 10.5 µg/L and ranging up to 92 µg/L. These levels in breast milk substantially exceed recommended infant doses that can be derived based on the Mass DEP RfD *as well as* both those advanced by NAS.

The presence of perchlorate in breast milk and various foods, along with limited biomonitoring data collected by the U.S. Centers for Disease Control indicate that exposures to this compound are likely to be common. This data combined with the approximately 10-fold concentration of perchlorate from serum to milk that has been demonstrated to occur in animal bioassays raises significant concern about neonatal perchlorate exposure. Furthermore, based on a limited number of samples, the data suggest that perchlorate may also inhibit iodide transport into human breast milk. Because breast milk is the nursing infant's sole source of iodide and newborns are particularly sensitive to thyroid disruption due to their limited reserve capacity of thyroid hormones and developing thyroid function, reduced iodide levels in breast milk would increase neonatal sensitivity to perchlorate and other thyroid toxicants. Thus, perchlorate may present a double threat to nursing infants if their mothers are exposed, contributing to a reduced level of iodide available to the thyroid and inhibition of the thyroidal uptake of the iodide that is present. MassDEP has concluded that acceptable exposure levels for perchlorate should reflect the significant uncertainty and data gaps that exist relating to neonatal perchlorate exposures and toxicity attributable to nursing.

In part based on these data, MassDEP and the MassDEP/DPH Advisory Committee on Health Effects have concluded that an UF of 30, associated with the lower NAS RfD value, is the minimum that should be considered with this data. Taking the full range of uncertainties involved into account (e.g. including the short duration of the Greer study as well as several other uncertainties detailed in the following report) MassDEP has concluded that a total UF of 100 should be applied to account for variability in human sensitivity, uncertainty in the effect level and overall database deficiency[1]. Some members of the Mass DEP/DPH Advisory Committee on Health Effects indicated that an uncertainty factor of 300 could be supported and one suggested that 30 could be sufficient. Application of UF of 100 or 300 to the Greer data

[1] MA DEP's uncertainty factor choices are consistent with guidance from the US EPA (2002c), as well as from previous NAS committees who specifically evaluated the use of uncertainty factors in the development of drinking water guidance (National Research Council , 1980; National Research Council , 1986).

yields RfDs of 7 x 10^{-5} mg/kg-day and 2.3 x 10^{-5} mg/kg-day, respectively. A UF factor of 30 would yield an RfD of 2.3 x 10^{-4} mg/kg-day. MassDEP notes that, in recognition of the significant gaps in the toxicology database for perchlorate, the NAS report recommended that numerous additional studies be performed[2]. Data from these studies may ultimately help to reduce the current uncertainty on perchlorate exposure risks.

In summary, the human data can be interpreted, depending on how the fundamental uncertainties in the scientific data are addressed, to support RfDs of 2.3 x 10^{-4} mg/kg-day (based on the NAS lower value and also viewed as reasonable by one member of the MassDEP/DPH Advisory Committee on Health Effects); 7.0 x 10^{-5} mg/kg-day (MassDEP's recommended value, which all members of the MassDEP/DPH Advisory Committee on Health Effects supported) or 2.3 x 10^{-5} mg/kg-day (which some members of the MassDEP/DPH Advisory Committee on Health Effects indicated could be supported). RfDs derived from the animal data fall within a similar range (2.8 x 10^{-5} to 8.5 x 10^{-5} mg/kg-day, see main report). Based on the weight of the evidence MassDEP has concluded that an RfD value of 7.0 x 10^{-5} mg/kg-day, based on the Greer study data and a composite uncertainty factor of 100, provides a scientifically defensible basis for evaluating exposures. The MassDEP/DPH Advisory Committee on Health Effects unanimously concurred with this decision. The U.S. Environmental Protection Agency (US EPA) recently adopted the NAS higher RfD value (7.0 x 10^{-4} mg/kg-day), which is now included on the Integrated Risk Information System database. In part based on the new data on perchlorate in breast milk, MassDEP scientists and the MassDEP/DPH Advisory Committee on Health Effects unanimously concluded that this value did not fully account for the uncertainties surrounding science's understanding of perchlorate toxicity and exposures.

In the derivation of health based drinking water values, MassDEP considers the RfD, other sources of exposure, receptor body weight, and water ingestion rates. With respect to other sources of exposure, the available data indicates that perchlorate is frequently found in foods including many types of lettuce, store milk, fruits and other vegetables. To account for exposures to perchlorate from these foods, as well as data that indicates that perchlorate may be concentrated into breast milk, MassDEP is applying a 20% relative source contribution factor in its drinking water value derivation. This choice is consistent with how MassDEP has dealt with this issue in the derivation of drinking water guidelines and limits for other chemicals based on non-carcinogenic endpoints.

When the RfD values in the range noted above are translated into drinking water values, apportioning 20% of the acceptable dose to drinking water, the associated health based drinking water values are as follow:

Uncertainty Factor	RfD (mg/kg-day)	Drinking Water Limit (ppb)
10	7 x 10^{-4}	4.9
30	2.3 x 10^{-4}	1.6
100	7 x 10^{-5}	0.49
300	2.3 x 10^{-5}	0.16

[2] MA DEP and the Advisory Committee on Health Effects also noted that the NAS' extensive proposed research agenda serves to highlight fundamental uncertainties in the science on perchlorate toxicity and support a health-protective approach in deriving acceptable exposure limits to protect children's health.

The value of 0.49 µg/L is associated with MassDEP's recommended RfD[3]. The highest value, 4.9 µg/L, is derived from the NAS RfD, which is not supported by MassDEP or the MassDEP/DPH Advisory Committee on Health Effects. One member of the MassDEP/DPH Advisory Committee on Health Effects indicated that the NAS lower RfD alternative was reasonable. This RfD is associated with a drinking water value of 1.6 µg/L. Several members of the MADEP/DPH Advisory Committee on Health Effects suggested that a lower RfD could be derived, which would lead to a drinking water value of 0.16 µg/L, but viewed the MassDEP final RfD as appropriate.

In selecting final drinking water standards, Mass DEP considers the RfD, as well as additional factors. These additional factors include the frequency of contamination, analytical limitations, treatment options, costs, and for contaminants like perchlorate that may be introduced into drinking water as a result of treatments to address pathogens, comparative risks.[4]

In summary, MassDEP is recommending an RfD for perchlorate of 7.0×10^{-5} mg/kg-day, based on the Greer study data and a composite uncertainty factor of 100.

[3] Values for the bottle-fed infant, using infant exposure parameters, are 0.44 µg/L using the MA DEP RfD.
[4] MA DEP's previous drinking water advisory level of 1 ppb was based on the department's recommended RfD and a method reporting limit of 1 ppb, based on a modification of US EPA Method 314, which was then in effect. Improved analytical methods have now reduced detection limits to below 1 ppb.

1.0 INTRODUCTION

The Massachusetts Department of Environmental Protection's (MassDEP's) work on perchlorate began in 2002 when high levels of the chemical were detected in the groundwater on Cape Cod. Groundwater at the Massachusetts Military Reservation (MMR) contained perchlorate levels as high as 500 ppb, and 3 nearby public drinking water wells serving the town of Bourne were contaminated with levels in the low parts per billion range. Due to the fact that there were no federal or state standards for perchlorate, at the request of the Bourne Water District, MassDEP provided interim advice on drinking water, which stated that if levels of perchlorate exceed 1 ppb, that sensitive subpopulations should not consume the water. Sensitive subpopulations were defined as pregnant women, infants, children up to age 12 and individuals with hypothyroidism. MassDEP's Office of Research and Standards (ORS), a toxicology and risk assessment unit, based the interim guidance on the most current scientific studies that were presented in the U.S. Environmental Protection Agency's (US EPA) 2002 (2002a) draft health assessment for perchlorate.

In January 2003, MassDEP made a decision to set standards for perchlorate due to the need to clean up sources on Cape Cod and to protect the public health. Using established protocols, MassDEP ORS initiated an in-depth review of the scientific information on the toxicity of perchlorate towards establishing a reference dose (RfD), the starting point for setting standards to protect public health. The perchlorate standards that MassDEP intends to set are cleanup standards to support the state's hazardous waste site clean up program as well as a drinking water standard. As part of the regulation development effort, MassDEP has also collected test data on the occurrence of perchlorate in public water supplies in Massachusetts. The results indicate that approximately 1% of the public water systems contain perchlorate at levels greater than 1 ppb and as high as 1300 ppb.

As part of its RfD derivation process, MassDEP held three meetings of its MassDEP/DPH Advisory Committee on Health Effects, an external scientific peer review group, along with scientific representatives of the U.S. Department of Defense, on the toxicity of perchlorate. Information and comments received from these meetings were taken into account in the assessment and derivation of a draft RfD. In establishing the draft RfD, MassDEP utilized a weight of evidence approach where the available data on perchlorate toxicity was critically evaluated for consistency and biological plausibility in order to select an appropriate point of departure to derive an RfD for this compound that is appropriately health protective for all members of the population.

In its 2004 toxicity assessment, MassDEP noted that the concordance of effect levels observed for several endpoints, including iodide uptake inhibition, hormone effects and brain morphometry, as well as the consistency in observed effects with those that would be expected based on the proposed mode of action provides a strong basis for establishing an RfD. Mass DEP's assessment included consideration of both the human and animal data to ensure that the impacts of perchlorate on various life stages are taken into account. Whereas the human data (e.g. Greer et al., 2002) represents the effects of perchlorate on healthy adults (iodide uptake

inhibition) the available data is insufficient to directly address risks to sensitive groups. The animal data (e.g. Argus Research Laboratories, 2001) addresses the effect of perchlorate on the fetus and neonates who have limited thyroid hormone synthesis capacity. MassDEP's final draft document, "Perchlorate Toxicological Profile and Health Assessment" contained a recommended RfD of 3×10^{-5} mg/kg-day based on studies of the effects of perchlorate in animals (iodide uptake inhibition, alterations in hormone levels, and brain morphometry) and in humans (iodide uptake inhibition).

After MassDEP's effort to set perchlorate standards was well underway, US EPA's work on its draft health assessment for perchlorate was suspended and a federal level decision was made that the draft would be reviewed by a special committee under the National Academy of Sciences (NAS). The charge of the NAS Committee was to evaluate the scientific studies conducted on perchlorate and to assess the draft 2002 US EPA health assessment report.

In January 2005, NAS released its report, *Health Implications of Perchlorate Ingestion.* The report includes recommended RfD values, which was unexpected since this was not a task within the charge of the committee. The NAS Committee was not unanimous in its view of the RfD with the majority recommending an RfD value of 7×10^{-4} mg/kg-day. One dissenting member of the committee thought the RfD should be 3 times lower, or 2.3×10^{-4} mg/kg-day. The NAS recommended RfD values are approximately 7 and 20 times higher than MassDEP's 2004 recommended RfD.

To ensure that MA standards on perchlorate reflect current scientific data, MassDEP has reviewed the NAS report and recommendations as well as additional data on perchlorate including data on perchlorate in breast milk that was not available during the NAS review. Mass DEP's process for undertaking this review included a preliminary discussion with members of its external scientific advisory committee in late January 2005 and a meeting with members of the committee in mid-February 2005 to receive input and advice. Two NAS Committee members also attended the February meeting to share their perspectives on perchlorate with MassDEP and its Advisory Committee on Health Effects.

The following report updates MassDEP's draft perchlorate toxicological assessment and RfD derivation (MassDEP, 2004), based on MassDEP's consideration of the NAS's perspectives and views, new data on perchlorate in breast milk, recently published studies and feedback received from its external scientific review committee. In keeping with MassDEP's weight of the evidence approach to deriving an RfD for perchlorate, the report first addresses the use of the human data from the Greer study to derive an RfD, followed by further assessment of the animal data. A range of possible RfDs and potential drinking water values associated with these RfDs is derived based on other sources of exposure and dosimetry adjustments.

2.0 CALCULATION OF A REFERENCE DOSE FOR PERCHLORATE

2.1 HUMAN STUDY POINT OF DEPARTURE - GREER ET AL. (2002)

There are six primary human exposure studies involving perchlorate (Table 1). The study of Greer et al. (2002) is the most complete and has been chosen as the most suitable for development of a point of departure from the human studies. This was a 14-day exposure study involving a total of 37 healthy, euthyroid adult subjects. They were assigned to 4 perchlorate dose groups of 0.007, 0.02, 0.1, and 0.5 mg/kg-day perchlorate and given perchlorate daily in drinking water for 14 days. In 24 of the 37 subjects, 8- and 24-hour measurements of thyroidal ^{123}I uptake (RAIU) were made before exposure, on exposure days 2 and 14 and 15 days after exposure ceased. Both the day 2 and 8-hour measurements on post-exposure day 15 were omitted in another group of 13 subjects who were otherwise treated the same as the first group. Each group's pre-exposure baseline served as its own control. The results for the 24-hour RAIU measurements on day 14 of exposure have been chosen for further analysis and are presented in Figure 1. RAIU decreased relative to the baselines in the 3 highest doses. The low dose group had an 8 % decrease from the baseline mean, based upon only seven individuals. Greer et al.'s analysis determined that the small response seen in the low dose group was not statistically significantly different from the baseline for that group. Based upon this conclusion for the low dose, Greer et al. (2002) designated this dose of 0.007 mg/kg-day as a NOEL, a no observed effect level, even though they presented a more refined analysis which suggested that the true effect level was likely lower. This designation was subsequently seconded in an independent analysis of the Greer paper by the NAS peer review Committee (National Academy of Science, 2005).

MassDEP supports the designation of RAIU inhibition (iodide uptake inhibition or IUI) as a critical effect and point of departure (POD) for the development of an oral RfD for perchlorate. Our position is consistent with U.S. EPA policy for setting RfDs (U.S. Environmental Protection Agency, 2002). The critical effect is defined as the first adverse effect, or its *known precursor*, that occurs to the most sensitive species, as the dose rate of the agent increases. RfDs have been set based on precursor biochemical changes such as plasma or red cell cholinesterase inhibition for various organophosphates such chlorpyrifos and malathion and induction of liver enzymes such as for 1,4-dibromobenzene and other chemicals (U.S. Environmental Protection Agency, 2005).

While it has been argued that IUI is not an adverse effect (National Academy of Science, 2005) in adults, but rather a precursor to adverse effects, it most certainly would seem to have the potential to causally lead to adverse effects in some circumstances. In its report, NAS stated that iodide uptake would need to be inhibited to a level of 75% or more for extended periods in healthy adults in order to cause truly adverse effects. No experimental data or quantitative assessment was provided in support of this statement. To our knowledge no human data exists that demonstrates the level of iodide uptake inhibition necessary to cause downstream effects, especially for the sensitive subgroups. At this time the relationship between IUI and thyroid hormone synthesis, especially in the fetus and neonate, is unknown. No pharmacodynamic model is available to address this issue. In fact, physiologically-based pharmacokinetic (PBPK) modeling combined with experimental data suggests that, in rodents, iodide uptake inhibition of

less than 2% may be associated with adverse effects on thyroid hormone status and, possibly, neurodevelopmental endpoints. Thus, there are no objective data addressing the degree of IUI that would lead to adverse downstream effects. Furthermore it is likely that this level would be variable. Clearly IUI is an element of perchlorate's mechanism of toxicity and not merely indirectly associated with its adverse effects. It may thus predispose individuals to sensitivity to other thyroid toxicants or conditions that impact iodide status, could lead to transient, but physiologically significant, changes in downstream parameters and/or could lead to adaptive responses that themselves may have impacts not yet understood. MassDEP believes that it is prudent and appropriate to functionally treat IUI as an adverse effect in deriving a health protective RfD. Thus, for purposes of the remaining discussion in this report we will refer to this endpoint in the Greer study as a LOAEL. Because the effect observed in the Greer study is not a frank adverse effect it is treated as a minimal adverse effect in the assessment. This is consistent with established protocols for deriving RfDs. The MassDEP/DPH Committee on Health Effects concurred with this determination.

In addition to the issues described in the preceding paragraphs, we consider the Greer study as statistically weak for deriving an RfD and examine the strengths and weaknesses of two approaches for deriving a perchlorate RfD in the following discussion. The first method is the NOAEL/LOAEL[5] approach and the second the benchmark dose approach.

2.1.1 NOAEL/LOAEL Approach To RfD Derivation

2.1.1.1 *NOAEL/LOAEL Characterization*

MassDEP and its Advisory Committee on Health Effects note that the designation of the low dose of 0.007 mg/kg-day as a NOAEL has several weaknesses based upon: i. statistical considerations; ii. shortcomings of analysis of group-averaged data; iii. strength of supporting observations from other studies.

Statistical Considerations

Viewed from a statistical perspective, the Greer study had very low power to detect significant differences from the baseline levels of RAIU. Given the limited number of individuals in the low dose group (7) and the variability observed in measured RAIU about the mean baseline (18.1%) for the low dose group (standard deviation of 8.2), it is possible to determine the magnitude of change from the baseline mean that would be detectable within an acceptable level of error. Sample size calculation approaches presented in Green (1979) and Sokal and Rohlf (1995) can be used to determine the difference from the baseline mean that is detectable with a given error risk (alpha level). The minimum difference that could be discriminated from the baseline mean was ± 40% with a 1-in-20 chance of being wrong. This range is represented by the shaded box in Figure 1. Given the limitations of the Greer study, it was unable to reliably detect up to a 40% inhibition of iodine uptake. This interpretation is consistent with that of the U.S. Environmental Protection Agency (2002a) in its draft report on perchlorate. They concluded that a NOAEL could not be identified from this study and they designated the lowest dose as a

[5] NOAEL – no observed adverse effect level;; LOAEL – lowest observed adverse effect level.

LOAEL. Their peer review panel supported this conclusion (U.S. Environmental Protection Agency , 2002b).

Greer and coauthors themselves actually performed a more refined analysis to help identify what they called the true NOEL from this experiment using linear regression of RAIU against the logarithm of the doses. They extrapolated the derived equation to identify the dose associated with 0% inhibition of RAIU as in the range of 0.005 – 0.006 mg/kg-day. The authors note, however, that due to variability in the data, inhibition of RAIU of from 8.3-9.5% is possible at this dose. This interpretation presents what the authors call the true (or predicted) NOEL as less than the experimental NOEL. Given the slope of the dose-response (DR) curve, inhibition at 0.007 mg/kg-day could exist. The U.S. EPA in their response to comments on their draft perchlorate assessment offered the criticism of this approach that they saw no *a priori* reason to assume that the shape of the dose response curve was linear in the zone of extrapolation below the low dose group response values.

Group Averaging

The majority of the analyses of the Greer study results by others have focused on the dose-group averaged response values for purposes of deriving a NOAEL-based RfD. Greer presented individual subject response data in his Figure 2 (see Figure 2 in this report). A differential response to perchlorate exposure appears to exist which is a function of the baseline level of iodide uptake. Those 3 or 4 individuals (their figure is not entirely clear on this point) in the low dose group whose baseline RAIU was above about 15% exhibited a greater degree of inhibition of RAIU (approximately 18-26%) than those who had baseline uptakes below this level (7% inhibition to 40% increase). One possible interpretation of this result is that even in the healthy adult population, there is variation in iodide uptake efficiency with those having higher uptake efficiencies being more affected by perchlorate exposure-induced iodide uptake inhibition. Greer et al. do not present data on serum iodide concentrations, which would enable one to determine whether this differential response was a function of an individual's baseline serum iodide level. If such a relationship exists, then applying these results to the rest of the population would suggest that those who might be iodine deficient either through diet, life stage or as a result of their reproductive status might be more susceptible to perchlorate-induced harm. Included in this group of concern are pregnant women, their fetus and neonates.

In their statistically-based evaluation of the Greer data with the benchmark dose (BMD) approach the U.S. Environmental Protection Agency (2003) characterized the iodide uptake responses of two of the possibly three individuals whose uptake efficiency increased as a result of low dose perchlorate exposure as outliers. They noted that some dose groups were more highly variable in their responses to perchlorate exposure and that removing the responses of these two individuals improved the homogeneity of variances in the sample set across doses. An alternative view is that perhaps these "outliers" had low baseline iodide uptake efficiencies and were relatively insensitive to perchlorate exposure. The absolute changes in RAIU in these individuals with low baseline uptakes were not large (1-4%) so that perhaps what was being seen was statistical "noise" rather than aberrant responses. The effect of censoring them from the data set would be to drive the estimates of effect at the low dose towards higher response levels and

more closely support an interpretation that this dose was indeed a LOAEL, rather than a NOAEL.

Supporting Data

MassDEP thinks that the strength of the evidence cited to support Greer et al.'s (2002) results warrants critical appraisal. A consistent picture of the nature of perchlorate-induced inhibition in iodide uptake and responses of thyroid hormones from the five other human perchlorate exposure studies has been cited as support for the designation of the low dose of 0.007 mg/kg-day as a NOAEL and POD for the derivation of an oral RfD (National Academy of Science, 2005). One of the five studies is a repeat of one of the published studies with a longer, although unspecified duration and was reported through a personal communication (Brabant, 1994). Two others are short, non-peer reviewed publications (Lawrence et al., 2001; Braverman et al., 2004[6]). All three of these contained limited descriptions of the studies, data and statistical analyses. Interpretation of these results is difficult as the raw data for some have not been available and some data are not published. Information from such incomplete communications is not of the standard normally relied upon as a significant basis for setting regulatory standards.

The Lawrence et al. (2001) reference is a letter to the journal editor and the Braverman paper is the abstract for a poster presentation at a professional meeting. Only one of the studies (Braverman et al., 2004) contained an exposure at the same dose level as the Greer low dose. The level of detail reported in the abstract for that work and in the actual poster for the work was insufficient for determining whether or not the reported conclusions of no effect of perchlorate exposure on RAIU and thyroid hormone status were supported by the data. That study's low dose level is subject to the same criticisms listed for the Greer et al. (2002) study, in which small sample size limited its ability to discriminate experimentally-induced differences from the baseline RAIU. If the low dose results from the Greer et al. (2002) study and the Braverman et al. (2004) study were to be pooled, there would still only be a total of 12 (7+5) individuals from which inferences about perchlorate's low dose effects on iodide uptake and thyroid hormone status can be drawn. However, with no data on intersubject variance reported for Braverman's study and no data on RAIU inhibition at early time points post exposure, MassDEP does not view that study as sufficient supporting evidence for the designation of a NOAEL.

2.1.1.2 *Accounting for Uncertainty to Derive a Human Study*-Based *RfD*

Although a total uncertainty factor of 300 can be supported, MassDEP is recommending that a total uncertainty factor of 100 be applied to the lowest dose in the Greer et al. study (2002). Application of an uncertainty factor of 100 represents a change from MassDEP's 2004 toxicological assessment where a total uncertainty factor of 300 was applied. In determining how to apportion the total uncertainty factor of 100, MassDEP is assigning an uncertainty factor of **10 for variability in human sensitivity** (consistent with NAS) and a value of **3 for a LOAEL to NOAEL adjustment**. The remaining factor of **3 accounts for database deficiency**. An uncertainty factor of 3 for database deficiency is consistent with the view of the

[6] This study has now been peer-reviewed and published in J Clin Endocrin Metab (April 24, 2006); however, MassDEP's critique of the study (i.e., small sample size, low statistical power) still holds.

dissenting opinion of one member of the NAS Committee[7]. The bases for these designations are discussed below.

Interindividual Variability (Sensitive Individuals)

This uncertainty factor accounts for the variation in responses to exposure to a chemical in the population and for the possibility (given a lack of relevant data) that the database available is not representative of the dose/exposure-response relationship in the subgroups of the human population that are most sensitive to the health hazards of the chemical being assessed (U.S. Environmental Protection Agency, 2002c). The full human variability uncertainty factor of 10 is applied by the NAS to the Greer low dose and will be maintained by MassDEP.

This factor for human variability is intended to account for differences in inter-individual sensitivity across all life stages (neonates, children or adults). The human short-term study was conducted in a limited number of healthy volunteers who were iodine-sufficient. The study groups do not represent the sensitive subpopulations (pregnant woman, fetuses, children, hypothyroid individuals, and people with thyroid disease). Justification for the use of a 10 fold UF in the derivation of reference doses can be found in Krasovskij (1976) and Dourson and Stara (1983). More information to justify the use of this uncertainty factor for perchlorate can be found in MassDEP's toxicity report (MassDEP 2004).

The U.S. EPA in its guidance on deriving RfDs (U.S. Environmental Protection Agency, 2002c) provides the advice shown in Table 2 for evaluating evidence about susceptible subpopulations. Several of their criteria are germane to the knowledge base for perchlorate where greater weight should be reflected in the assignment of a higher UF when: the effect occurs at greater magnitude in one or more life stages, when different types of effects are seen in specific subpopulations, and when the effects differ in seriousness or degree of reversibility in specific subpopulations. For perchlorate, it is recognized that the pregnant mother, her fetus and the neonate are at particular risk from perchlorate-induced iodide deficiency. Since at these life stages, iodide deficiency may already exist in the absence of perchlorate exposure, added deficits as a result of perchlorate exposure could be beyond the compensatory capabilities of these individuals to withstand excursions in available serum iodide and concomitant changes in thyroid and pituitary hormones. The fact that we don't fully know the perchlorate dose-response relationship for this susceptible subgroup argues for conservativeness in the assignment of a UF.

The possible dependence of the perchlorate-associated IUI on the baseline level of iodide uptake seen in the individual responses from the Greer et al. (2002) study can also be viewed as either representing the variability across the human population, or alternately a unique subpopulation response.

[7] "One NAS committee member thought that the factor for database uncertainty should be greater than one and provided the following rationale: The RfD is derived from a study in which a group of only seven healthy adults was given 0.007 mg/kg of perchlorate daily for 14 days (Greer et al. 2002). Although two other studies had similar results, the total number of subjects is still small. In addition to the small number of subjects, no chronic exposure studies have been published. An uncertainty factor of 3 could account for the uncertainty surrounding the small number of subjects and the absence of a long-term study."

LOAEL to NOAEL Extrapolation

An uncertainty factor is normally employed in this category when the starting point for the derivation of an RfD is a LOAEL or LOEL in order to extrapolate the results based on effects observed at a low dose to the dose where no effect would be observed. MassDEP's view that the lowest dose in the Greer study (0.007 mg/kg-day) may not be a true no observed effect level has not changed. **MassDEP prefers to view this lowest dose as a minimal Lowest Observed Adverse Effect Level (LOAEL) and to maintain an uncertainty factor of 3**, for reasons developed in Section 2.1.1.1 (low study power to detect an effect, positive individual inhibition responses at the NOAEL obscured by group-averaging, and a lack of good low dose corroborating data) and as further described in MassDEP's 2004 draft toxicological assessment (MassDEP, 2004).

Derivations of RfDs take into account the nature of the critical effect, such as whether it is a biochemical change versus a frank adverse effect and whether the effect is on the causal pathway to more serious effects by way of an uncertainty factor. For example, when deriving an RfD that is based on a precursor effect, the uncertainty factor to extrapolate from a lowest observed adverse effect level to the no observed adverse effect level may be lower (e.g., three-fold) than if you were starting with frank effects such as brain damage (e.g., ten-fold).

When the responses of seven healthy individuals to perchlorate exposure are examined, it is apparent that even at low perchlorate doses, there are some individuals whose uptake of iodine can be substantially affected by perchlorate exposures. This observation calls into question the designation of 0.007 mg/kg-day as a NOAEL. An alternative analysis of the perchlorate dose response data from the Greer et al. (2002) study by the U.S. EPA (benchmark dose analysis) identified a BMDL dose of 0.002 mg/kg-d which suggests that biologically significant inhibition of iodine uptake can't be ruled out at a dose of 0.007 mg/kg-day (U.S. Environmental Protection Agency, 2003).

Database Insufficiency

This factor may be employed to adjust a NOAEL or LOAEL downwards to reflect the level of uncertainty in the database for the chemical. **MassDEP is recommending an uncertainty factor of 3 for database deficiency** due to concerns over:

(1) lack of chronic data. The duration of exposure in the Greer study was only 14 days, during which time iodide uptake inhibition of the thyroid was measured. Long-term effects due to iodide uptake inhibition, thyroid accumulation of perchlorate, thyroid hormone perturbation, or direct chronic effects of perchlorate in various other organs cannot be determined from this study. No oral chronic studies at this low dose level exist;
(2) emerging data indicating potentially widespread contamination of breast milk by perchlorate and related uncertainties regarding the degree to which perchlorate may interfere with iodide transport into breast milk, which could increase the sensitivity of the

neonate to perchlorate thyroid disruption, and data that indicates perchlorate may be concentrated into breast milk (see more detailed discussion in Sections 3.1 and 3.2)[8].

In addition, there is limited information on the interactive effects of perchlorate with other goitrogenic chemicals in the environment, such as nitrate.

Two other reviewers of the human perchlorate exposure literature (California Environmental Protection Agency, 2004; National Academy of Sciences, 2005) have concluded that, if the initial step of perchlorate-induced inhibition of thyroid uptake of iodide is limited, then the potential succeeding events that could lead to thyroid hormone changes and subsequent neurodevelopmental effects in offspring of mothers exposed to perchlorate or neonates directly exposed to perchlorate, will be prevented. This conclusion seems to reflect an assumption that pregnant women and the neonate, who in some cases may already be iodine deficient or have lower iodine reserves to supply hormone production needs during periods of perchlorate-induced iodine deficiency, will respond in the same way as healthy adults to perchlorate exposure. MassDEP has seen no data or argument that supports this assumption. There is a significant gap in our knowledge of how much IUI these susceptible subgroups can withstand and by extension, how they will respond to low-level perchlorate exposures.

2.1.2 Benchmark Dose Approach

Analysis of dose-response data with the benchmark dose approach has been coming into greater use in regulatory toxicology since its earlier introduction by authors such as Crump (1984) and Barnes and Dourson (1988). Setzer and Kimmel (Setzer et al., 2003) provide a more recent perspective on its use and note that it has the advantages over the NOAEL/LOAEL approach of using the entire set of data over all doses tested and as being more transparent and quantitative. It models the dose response curve in the range of observable data and then uses a model to predict the dose associated with a chosen level of response – the benchmark dose (BMD) (e.g., 5 or 10%). Confidence limits can be calculated and the lower confidence limit on the dose used as the BMD is called the BMDL. This BMDL value is used as the point of departure for calculation of an RfD. Unlike the NOAEL, especially as designated from the Greer et al. (2002) study, the BMDL accounts for the uncertainty in the estimate of the dose response that is due to the characteristics of the experimental design such as sample size.

[8] The detection of perchlorate in breast milk raises several issues. First of all, the degree to which it may interfere with iodide transport into the milk, which may *increase the sensitivity* of the neonate to the direct action of thyroid toxicants, including perchlorate, is a concern that has not been adequately addressed to date. The data suggesting that perchlorate may furthermore be concentrated into breast milk also raises a related but separate concern regarding *overall exposure levels to the neonate* (see Section 3.1 and 3.2). Neonate exposures to perchlorate in breast milk could ultimately be accounted for through the use of a quantitative adjustment to the maternal RfD to ensure that maternal to neonatal exposures do not exceed acceptable levels. However, sufficient data to do this is not currently available. Alternatively, an additional UF could be applied in the derivation of the maternal RfD and/or adjustments made to the proportion of the total maternal perchlorate exposure allowed from drinking water. As is discussed above and in section 3.1 and 3.2, MA DEP has concluded that the uncertainty regarding perchlorate's effect on iodide transport into milk provides partial support for the use of a database deficiency uncertainty factor. Uncertainty in perchlorate's concentration into breast milk supports the use of a conservative relative source apportionment factor to limit potential neonatal exposures from breast milk.

In cases where there are either problems or difficulties with the NOAEL/LOAEL approach for RfD derivation such as with perchlorate, the BMD advantages can be attractive. The challenge with using a BMD analysis on the Greer data is getting agreement on a POD for RAIU inhibition.

The U.S. EPA (U.S. Environmental Protection Agency, 2003) in its response to comments on its 2002 draft evaluation of perchlorate's effects and California (California Environmental Protection Agency , 2004) performed benchmark dose analyses on the Greer et al. (2002) data. US EPA censored two of the data points for the low dose group for statistical reasons and identified a BMDL 0.002 mg/kg-day for a 5% response rate. Irrespective of whether one calls a 5% response a no effect level or low effect level, the implication of this analysis is that the 0.007 mg/kg-day of the Greer et al. study is not a no effect level.

California's BMD analysis employed the U.S. EPA's BenchMark Dose analysis software, Ver. 1.3.1 and found the Hill model provided the best fit to the data, similar to EPA's conclusion. A BMDL of 0.0037 mg/kg-day was identified as a POD for the development of a RfD. This dose, like that identified by EPA with censoring, was below the NOAEL of 0.007 mg/kg-day identified by Greer et al. (2002) and NAS (2005) for this data set. It should be noted that the basis for the choice of a 5% response level in the modeling was to have a minimal biologically significant change as a point of departure.

The conclusion that MassDEP derives from these BMD analyses of the Greer et al. (2002) data is that a dose of 0.007 mg/kg-day cannot be confidently declared a no effect level for perchlorate exposure. This fact should be recognized either by designating the 0.007 mg/kg-day dose as a minimal LOAEL and assigning a partial amount (3) of the total UF (10) which could be assigned for extrapolating low effect data to a no effect level, or by employing a BMDL as the POD for assignment of uncertainty factors.

2.1.3 MassDEP Recommended Derivation of a Reference Dose Based Upon Human Data

The low dose of 0.007 mg/kg-day in the Greer et al. (2002) study is chosen as the point of departure for derivation of an RfD based upon human data. For a variety of reasons including poor statistical power of the study, the strong positive responses seen at this dose in some of the small study group and the weakness of potentially corroborating data for calling this a NOAEL, MassDEP views this dose as a minimal LOAEL.

The following uncertainty factors can be applied to adjust this dose downwards to an RfD such that it should be protective of all members of the human population:

10 - for sensitive individuals
3 - for minimal LOAEL to NOAEL extrapolation
3 - for database insufficiency.
100 TOTAL UF

$$\text{RfD} = \frac{0.007 \text{ mg/kg-day}}{100} = \mathbf{7 \times 10^{-5} \text{ mg/kg-day.}}$$

An alternative and supportable interpretation would be to apply a full factor of 10 for database insufficiency as has been recommended by some of our peer review committee members to produce a total UF of 300 and associated RfD of **2.3 x 10^{-5} mg/kg-day**:

10 - for sensitive individuals
3 - for minimal LOAEL to NOAEL extrapolation
10 - for database insufficiency
300 TOTAL UF

$$RfD = \frac{0.007 \text{ mg/kg-day}}{300} = \mathbf{2.3 \times 10^{-5} \text{ mg/kg-day}}$$

The lower of the two NAS RfDs, which relied on a total UF of 30 and which was supported by one member of the NAS Committee and one member of our Committee was **2.3x10^{-4} mg/kg-day.**

10 – for sensitive individuals
3 – for database uncertainty
30 TOTAL UF

$$RfD = \frac{0.007 \text{ mg/kg-day}}{30} = \mathbf{2.3x10^{-4} \text{ mg/kg-day.}}$$

2.2 USE OF ANIMAL STUDIES FOR SUPPORTING AN RfD BASED ON HUMAN DATA

2.2.1 Background

Information on the toxicity of perchlorate on the most sensitive subgroups of the human population is inadequate. Data on iodine deficient populations as well the mechanism of action believed to be responsible for perchlorate toxicity indicate that the most sensitive subgroups of the population for iodine deficiency are:

- pregnant women especially when marginally iodine-deficient or iodine-deficient,
- fetuses and infants of these women,
- premature infants,
- children, and
- hypothyroid individuals.

Due to a lack of adequate data on the toxicity of perchlorate in the sensitive subgroups, various rodent studies were conducted in the late 1990s and early 2000 to fill data gaps (U.S. Environmental Protection Agency , 1998a, 2002a). These studies are extensively discussed in the 2004 draft MassDEP perchlorate health assessment document (MassDEP 2004).

2.2.2 Justification for Use of Animal Data in the Weight of Evidence Assessment and RfD Designation Process

MassDEP is considering the rodent studies as supporting evidence in the perchlorate risk assessment process because: (1) the rat may be a good model to represent the most sensitive subgroups, especially the iodine deficient pregnant woman and the congenitally hypothyroid fetus which may depend only on maternal thyroid hormones during *in utero* development; (2) sensitive subgroups are being directly tested (the pregnant rat and its fetus and the neonate); and, (3) the observed results in the animals are consistent with the proposed mode of action of perchlorate, including the upstream effect of iodide uptake inhibition followed by downstream effects such as thyroid and pituitary hormone perturbations and thyroid and brain structural alterations. Appendix A contains further information on the justification for using the animal studies as supporting evidence in the derivation of an RfD for perchlorate.

2.2.3 Studies Conducted in Rats at Different Life Stages

The studies of perchlorate toxicity in animals demonstrated the following effects consistent with its proposed mode of action of perchlorate:

- inhibition of iodide uptake (Yu et al. 2000);
- decrease of serum T4 and T3 levels and increase of TSH levels (Caldwell et al. 1995; Springborn Laboratories, 1998; Argus Research Laboratories, 1998a,b, 2001);
- thyroid hypertrophy (increased cell size), hyperplasia (increased cell number) across life stages, and tumors[9] in F1 generation rats (rats exposed *in utero* and throughout lactation)[10] (Caldwell et al. 1995; Argus Research Laboratories, 1998a,b);
- alteration in brain morphometry (form and structure) and behavior in rat pups that were exposed *in utero* and after birth (Argus Research Laboratories,1998b, 2001; Bekkedal et al. 2000).

2.2.4 Critical Study (Argus Research Laboratories, 2001)

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[9] It is suggested that thyroid cancer in humans resulting from perchlorate exposure is unlikely, since rats are sensitive to the development of thyroid tumors because their thyroid function is easily disrupted. Based on this argument, humans are much less susceptible than rats to disruption of thyroid function and, therefore, are not likely to develop thyroid tumors as a result of perchlorate exposure (NAS, 1995). The comparative sensitivity of humans and rats is discussed Appendix A. The database on long-term effects of perchlorate either on the sensitive population or the general population is insufficient to make such conclusions. A number of studies (Pendergast et al., 1960, Wahner et al., 1966; Williams et al., 1977; Williams, 1985; Levi et al., 1991; Pettersson et al., 1996; Vigneri et al., 1998) conducted in various parts of the world found that iodine deficiency may increase the incidence of thyroid malignancy and alter the type of cancer produced. Since perchlorate can contribute to functional iodine deficiency, its ability to cause thyroid cancer cannot be ruled out. Moreover, perchlorate was found to be a potent promoter of thyroid tumors in animals (Hiasa et al. 1987) and its effect in people with already initiated tumors is unknown. Based on its mode of action, perchlorate has the potential to contribute to thyroid tumors at doses sufficient enough to decrease thyroid hormone levels and change thyroid structure.

[10] Perchlorate was found to be nongenotoxic in various *in vitro* and *in vivo* studies, suggesting that the mechanism of tumor formation might be perturbation of the thyroid and pituitary hormone homeostasis (ManTech Environmental Technology , 1998; Zeiger, 1999).

Of the above listed studies, the critical study selected for perchlorate reference dose determination by MassDEP in 2004 and now in 2005 is the Argus (2001) neurodevelopmental study, which investigated sensitive endpoints at different life stages. In this study, perchlorate produced changes in pituitary and thyroid hormone levels and thyroid morphometry at different life stages. Brain mophometry changes were also reported, but these have been questioned due to experimental design and execution issues. The study is extensively discussed in the MassDEP (2004) document and is summarized below.

2.2.4.1 *Thyroid and Pituitary Hormone Alterations and Changes in Thyroid Structure*

Female Sprague-Dawley rats were treated with ammonium perchlorate at 0, 0.01, 0.1, 1.0, or 30 mg/kg-day in drinking water two weeks prior to cohabitation and continuing through the day of sacrifice. F1-generation pups were not directly dosed but might have been exposed *in utero* during gestation and via maternal milk and maternal water during the postpartum period. Significant changes were observed in thyroid and pituitary hormone levels at the lowest dose at different life stages (Table 3). Thyroid histopathology was also altered in both dams and pups, although at higher doses.

2.2.4.2. *Brain Morphometry Changes*

Because thyroid hormones are important for normal neurodevelopment, the Argus (Argus Research Laboratories , 2001) study also investigated treatment-related changes in brain morphometry. Significant changes, especially in the corpus callosum and striatum, were observed at the lowest dose. Similar changes in various brain regions, especially in the corpus callosum and striatum, were also observed in the Argus (Argus Research Laboratories, 1998a) study. These are summarized in Appendix B. However, various reviewers of the 2002 US EPA perchlorate toxicity document have challenged the brain morphometry data, especially the plane of cut of the corpus callosum, leading to considerable uncertainty in the quantitative interpretation of this data. . The NAS also reviewed several studies to establish biological plausibility of the effects of perchlorate on the corpus callosum, and concluded that although not widely recognized as a classic marker of neonatal hypothyroidism, increased thickness of the corpus callosum appears to be a biologically plausible effect. Based on the NAS report and further input from the MassDEP/DPH Advisory Committee on Health Effects, MassDEP has concluded that the brain morphometry data should not be quantitatively used in the derivation of an RfD. That data does however qualitatively support concern over perchlorate neurodevelopmental toxicity.

2.2.5 MassDEP Selected Animal Endpoint For Supporting RfD for Perchlorate

Changes in thyroid and pituitary serum hormone levels have been detected in several perchlorate treated species (Table 4) at different life stages, indicating that the hormone changes (Table 3) observed in the critical study (Argus Research Laboratories , 2001) are not isolated incidents. The NAS report also concurred that hormone changes were observed in the animal studies.

One issue with the hormone data is that the effects observed may be of too low a magnitude (Table 3, Table 5) to cause any further downstream effects (NAS, 2005). However, small and transient changes in thyroid hormone levels in pregnant women have been associated with

neuropsychological impairments (Haddow et al. 1999, Klein et al. 2001), and brain structural changes in rats (Auso et al. 2004). These studies are discussed in detail in Appendix C.

MassDEP views changes in thyroid hormone status as an adverse effect and has used these as the POD for deriving animal-based RfD values.

2.2.6 Summary and Conclusions

Perchlorate treatment in rats produces changes in thyroid hormone levels, thyroid morphometry and thyroid tumors consistent with its proposed mode of action. In the 2004 MassDEP draft perchlorate health assessment, MassDEP selected the Argus (2001) study as the primary basis for its draft recommended RfD for perchlorate. MassDEP utilized this study since it provided information on the direct effects of perchlorate on sensitive subgroups. MassDEP is continuing to use information from this study as part of its weight of the evidence approach but as supporting evidence for the human data rather than a primary point of departure for an RfD. MassDEP is making this revision in part based upon the National Academy of Sciences report (NAS, 2005).

Due to the controversy surrounding the brain morphometry data, MassDEP has concluded that the significant changes in thyroid and pituitary hormone levels are the preferable endpoint to use. The lowest observed adverse effect level (LOAEL) for this endpoint is 0.01 mg/kg-day, and this value is used as a point of departure to derive animal based RfDs for perchlorate (in support of the human data) as discussed below.

2.2.7 Derivation of RfD Values Based on the Animal Data

MassDEP has derived possible animal-data based RfD values using total uncertainty factors of 100 and 300, applied to the LOAEL dose in the Argus Laboratory study (2001). MassDEP and the MassDEP/DPH Advisory Committee on Health Effects concluded that an UF of at least 100 was needed to account for the uncertainties inherent in the use of the animal data with some participants supporting a UF of 300. Thus, both UFs have been used in the following calculations. Use of an uncertainty factor of 100 represents a change from MassDEP's 2004 toxicological assessment where a total uncertainty factor of 300 was applied.

For the total UF of 300 the apportionment is the same as presented in DEP's 2004 assessment. In summary, uncertainty factors included values of:

- 10, applied to adjust the LOAEL. This is the standard approach used when a NOAEL is not available. The size of the LOAEL-to NOAEL uncertainty factor may be altered, depending on the magnitude and the response at the LOAEL (U.S. Environmental Protection Agency, 2002c). In this case, a factor of 10 was deemed appropriate given that effects on multiple endpoints were observed including impacts on thyroid hormone levels.
- 10, to account for variations in susceptibility within the human population (intra-human variability) and the possibility (given a lack of relevant data) that the database available is not representative of the dose/exposure-response relationship in the subgroups of the

human population that are most sensitive to the health hazards of the chemical being assessed (U.S. Environmental Protection Agency, 2002c).
- 3, to account for interspecies extrapolation.

In the case of the total uncertainty factor of 100, MassDEP apportioned this as follows:

- an uncertainty factor of 10 for the LOAEL to NOAEL adjustment
- a composite value of 10 to account for variability in human sensitivity and interspecies extrapolation. This reduction in the UF for these factors is appropriate if the NAS contention that the rodent model is particularly sensitive to perchlorate-induced alterations in thyroid hormone status is correct.

As discussed in preceding sections the NAS position on this matter is, however, open to question, in which case a total UF of 300 would be justified.

Applying a total UF of either 300 or 100 to the study LOAEL results in RfD values of 2.8×10^{-5} mg/kg-day and 8.5×10^{-5} mg/kg-day, respectively. The derivation of these values is presented below:

For total UF of 300:

10 - for sensitive individuals
10 - for LOAEL to NOAEL extrapolation
3 - for interspecies extrapolation
300 TOTAL UF

$$\text{RfD} = \frac{0.0085 \text{ mg/kg-day}}{300} = \mathbf{2.8 \times 10^{-5} \text{ mg/kg-day}}$$

For Total UF of 100:

10 - LOAEL to NOAEL extrapolation
10 - composite UF for sensitive individuals and interspecies extrapolation
100 TOTAL UF

$$\text{RfD} = \frac{0.0085 \text{ mg/kg-day}}{100} = \mathbf{8.5 \times 10^{-5} \text{ mg/kg-day}}$$

3.0 ASSOCIATED DRINKING WATER VALUES

Drinking water values (or health based limits for contaminants in drinking water) are derived by converting a dose of the chemical in question to a concentration in water using exposure parameters and apportioning a fraction of the total reference dose (the RfD or total dose of the chemical in question allowed from all sources per day per kilogram body weight) to the drinking

water pathway. Typically, drinking water values are calculated using a standardized approach based on a 70 kg adult consuming 2 liters of water per day. In some cases adjustments may be made to account for differences in water intake rates and body weights of infants, children and pregnant women as compared to other adults. Although no current drinking water standard reflects the breast milk exposure pathway, MassDEP notes that further adjustment for exposures to nursing infants may also be warranted as they may experience quantitatively different exposures to chemicals, such as perchlorate, that are expressed in breast milk.

3.1 RELATIVE SOURCE APPORTIONMENT FACTOR

US EPA guidance recommends the use of a source apportionment factor in the range of 20% – 80% in the derivation of drinking water values for chemicals where exposures are likely to occur through additional pathways (U.S. Environmental Protection Agency, 1998a). A source apportionment factor is needed in the case of perchlorate because other exposures are likely.

Specifically, perchlorate has been found in common food items. In a preliminary study by the US Food and Drug Administration, 116 out of 128 samples of four types of lettuce from California, Arizona, New Jersey, and Florida contained perchlorate ranging in concentration from 1-129 ppb. Of 104 samples of cow's milk from across the country, 101 contained perchlorate with concentrations ranging from 3.1-11.3 ppb (U.S. Food and Drug Administration, 2004). In a separate study perchlorate was detected in all seven brands of dairy milk randomly purchased from grocery stores in Lubbock, Texas (Kirk et al. 2003). Most recently, perchlorate was detected in 46 out of 47 dairy milk samples from 11 states, with an average concentration of 2 ppb (Kirk et al. 2005). Another study focused on the development of analytical methods tested for perchlorate in a variety of food products, e.g., fresh fruits, vegetables, milk, alcoholic beverages, baby foods and other products harvested or processed in many parts of the world. The analysis showed the presence of perchlorate in most food products. Higher perchlorate levels were found in products from California (e.g., green grapes having 19 ppb), Mexico (e.g., 62.8 ppb in red tomato and 39.9 ppb in asparagus), and some South American countries, with cantaloupe from Guatemala having approximately 463 ppb of perchlorate. Foods produced in Canada and China showed the lowest level of perchlorate. Food products from Europe also showed relatively low perchlorate levels. The study also found that perchlorate can survive in food even after processing at a high temperature (El Aribi and Sakuma 2005). Although the data is limited, other food items are also likely to contain perchlorate. Recently, a Texas Tech investigator found perchlorate in samples of commercially grown wheat and alfalfa. In this study perchlorate concentrations ranged into the ppm range, considerably higher than those observed in the studies previously mentioned on lettuce and milk (Jackson et al. 2005). Although the database is limited for quantifying food and beverage perchlorate exposures, it does appear that perchlorate may be very pervasive in the U.S. food supply (U.S. and imported products). Concerns about exposures to perchlorate due to food ingestion are also supported by a recent study conducted by the U.S. Centers for Disease Control (CDC) on perchlorate in urine (Valentin-Blasini et al. 2005). CDC analyzed urine samples collected anonymously from healthy adult donors from Atlanta, Georgia, an area with no known perchlorate drinking water contamination. The limited sampling event of only 61 samples produced results showing that perchlorate was detectable in all of the urine samples ranging from 1 to 35 μg of perchlorate/g of creatinine.

The available human data also indicate that neonatal exposures to perchlorate in breast milk are likely to be widespread. Perchlorate has been detected in the breast milk of subjects from the Chilean cities of Chantaral at 19 µg/L (ppb) (where the water concentration was 5-7 µg/L (ppb)) and in Taltal at 104 µg/L (ppb) (where the water concentration was 100-120 µg/L (ppb)). Data also demonstrates that perchlorate is also common in breast milk in the US. In the study noted above, breast milk samples from all 36 individuals tested contained perchlorate. The maximum concentration was 92 µg/L with an average concentration of 10.5 µg/L (Kirk et al, 2005). The individuals tested were from 18 states indicating that perchlorate contamination of breast milk is likely to be widespread. These data indicate that breast-fed neonates may experience significant perchlorate exposures from breast milk. Neonatal consumption of breast milk with the average concentration of perchlorate reported in the Kirk et al study would result in exposures that exceed both the RfD values recommended by the NAS, as well as that recommended by Mass DEP.

Thus, the available data clearly demonstrates that perchlorate is prevalent in common foods and suggests that exposures to perchlorate from such consumables may be substantial. In addition, other dietary and environmental thyroid toxicants acting through a similar mechanism (e.g. nitrate) exist and will contribute to overall levels of thyroid disruption. Mechanistically, exposures to all such agents should be considered. Unfortunately the data is insufficient at this time to derive population-based exposure distributions from consumption of other perchlorate containing food items or to evaluate aggregate exposures to other thyroid toxicants.

In situations where other exposures are likely but the data is insufficient to quantitatively evaluate the relative contributions of other sources, federal and state drinking water programs often use a 20% source apportionment factor in drinking water limit derivations. In such situations, MassDEP has consistently used 20% in all of its drinking water guidelines based on non-cancer endpoints. Given the available data, MassDEP has concluded that a 20% factor is appropriate in the case of perchlorate.

3.2 ADJUSTMENTS FOR NEONATAL EXPOSURE

MassDEP scientists and members of the MassDEP/DPH Advisory Committee on Health Effects have noted that perchlorate risks to neonates are of particular concern due to their limited reserve capacity of thyroid hormones, incompletely developed thyroid functions, and higher liquid consumption rate per unit of body weight (of water in formula and/or breast milk). Although a concern, MassDEP did not focus on the issue of neonatal dosimetry in its earlier 2004 Draft Assessment because the proposed drinking water limit guideline of 1 ppb was determined by analytical limitations. Adjustment for neonatal dosimetry would have resulted in values below this limit, in which case the final guideline would still have defaulted to the analytical based reporting limit of 1 µg/L (ppb) in drinking water. In light of the higher RfDs proposed by the NAS and the data on perchlorate in breast milk, MassDEP has revisited this issue.

The US EPA in their 2002 draft assessment concluded that dosimetric adjustment for neonates was not needed in the case of perchlorate because the available PBPK models indicated that infant internal doses would likely be less than those of adults at a given exposure. Thus, for

water at a given perchlorate concentration, although infants would be expected to consume a greater daily dose of perchlorate on a per kilogram body weight basis, other pharmacokinetic factors (such as protein binding levels; kidney clearance rates; volumes of distribution etc.) would be expected to reduce the resulting delivered dose and IUI in the infant compared to the adult. MassDEP, however, notes that the available PBPK data supporting this position are by no means definitive because the models have not to date been fully developed or verified with respect to the human fetus and neonate.

The pharmacokinetics of toxicants vary considerably across life stages and across species. Of particular relevance to this discussion is the fact that very significant changes in pharmacokinetic functions occur during fetal and neonatal development and these vary considerably between rodent and human neonates (Ginsberg et al. 2002). Although the NAS did not address the issue of neonatal dosimetry adjustment in their report (NAS, 2005), they also noted limitations of the PBPK modeling data, stating:

> "Although no formal sensitivity analysis was performed on the human PBPK model, it is likely that, in addition to the skin compartment, urinary clearance of both [*sic*. perchlorate and iodide] and the plasma-protein binding of perchlorate may be important for additional future research. Furthermore, the PBPK model was developed for adult males and females (primarily healthy subjects although one subject with Graves disease was simulated) but not for pregnant or lactating females, human fetuses, neonates or children." (MassDEP note: the model under-predicted iodide uptake inhibition in the Graves disease patient modeled) and,
>
> "Given the important species differences in developmental biology and the current inability to validate extrapolation to human fetuses and neonates, such an approach (PBPK modeling) should be used with caution for these potentially sensitive populations."

The uncertainties in the PBPK models raise significant doubts regarding the use of the rodent neonate model outputs to conclude that human neonate internal doses will be less than in adults for a given intake. This is clearly an area where further research is needed. Given the available data MassDEP has concluded that it is appropriate to consider the default assumption of equal dosimetry in infants and adults (i.e., that the neonate will receive the same internal dose per unit of ingested dose as the adult) which necessitates adjustment of human infant exposures to account for their higher consumption of fluids per body weight compared to adults (and thus higher total ingested dose).

MassDEP notes that US EPA has previously included neonatal dosimetry adjustment in the derivation of a drinking water standard (for nitrate). To provide consistency, MassDEP has concluded that the body weight and liquid intake parameters used in the derivation of the US EPA nitrate limit are appropriate for dosimetric adjustment for perchlorate as well. Thus, an infant BW of 4 kg and consumption rate of 0.64 L/day were used to assess neonatal exposures.

These values are in the range of those reported in the 2002 interim US EPA Child Specific Exposure Factor Handbook (U.S. Environmental Protection Agency, 2002d)[11].

Formula-fed Infants. In the case of formula fed infants, a 100% apportionment to the drinking water used to make formula was selected. This is clearly appropriate, as exposures due to other foods are not a concern.

As noted in Table 6, possible drinking water values derived using these parameters are only marginally lower than those calculated using adult body weight and water consumption rates with a 20% source apportionment value.

Breast fed-Infants. The situation in the case of a breast fed infant is more complex as one must derive an acceptable drinking water value for the lactating mother that appropriately accounts for the potential concentration of perchlorate into breast milk. As noted earlier, perchlorate is expressed into breast milk and may also inhibit iodide transfer into the milk[12]. Furthermore, animal data indicate that perchlorate may be *concentrated* into breast milk[13]. Breast feeding infant exposures to perchlorate will therefore reflect the total maternal perchlorate exposure and the degree to which it is concentrated into breast milk and may well, on both an absolute and an adjusted body weight basis, exceed the exposures experienced by adults consuming contaminated water. Therefore, to account for the potential concentration of perchlorate into breast milk and ensure that breast milk concentrations do not exceed levels acceptable for the neonate, total maternal exposures may need to be well below RfDs for adults.

With respect to neonatal exposures, an acceptable breast milk perchlorate concentration can be derived for any selected RfD value. For example, based on a 4 kg infant consuming 0.64 L of breast milk and using the lower of the two NAS RfDs (2.3×10^{-4} mg/kg-day, which is the highest RfD that MassDEP and its MassDEP/DPH Advisory Committee on Health Effects believe can be supported), the breast milk concentration of perchlorate would need to remain below 1.4 µg/L (ppb) to keep infant exposures below the RfD. Based on MassDEP's recommended RfD of 7×10^{-5} mg/kg-day, the breast milk value would be 0.42 µg/L (ppb). Based on the average breast milk concentration from the US samples of 10.5 µg/L, a 4 kg newborn consuming 0.64 L of milk per day would receive a dose of 1.68×10^{-3} mg/kg-day, exceeding the MassDEP RfD and both of the NAS RfD values (2.3×10^{-4} mg/kg-day and 7×10^{-4} mg/kg-day).

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[11] The 2002 interim US EPA Child Specific Exposure Factor Handbook (U.S. Environmental Protection Agency, 2002d) recommends a breast milk consumption rate of 0.74 L/day for 1-6 month old infants. The mean value for 1-month old infants was reported to equal 0.70 L/day. This reference presents smoothed 50th percentile body weights for one-month old male and female infants as 4.29 and 3.98 kg, respectively.

[12] Based on a *very limited* number of samples from this study population, for breast milk samples with a perchlorate content greater than 10 µg/L, the iodide content of the breast milk (the nursing infants sole source of iodide) was reported to be inversely proportional to the perchlorate concentration (r^2 of >0.9; $n = 6$) (Kirk et al. 2005). Thus, nursing infants may be subjected to a "double insult" if their mothers are exposed to sufficient perchlorate; a reduced level of iodide available to the thyroid and inhibition of thyroidal iodide uptake by perchlorate.

[13] The perchlorate concentration in the milk of lactating rats exposed to a perchlorate dose of 0.01 mg/kg-day was close to 10-fold higher than the concentration in the maternal serum (Clewell et al. 2003, Fig 2 panels A and E). In this case the PBPK model under predicted the observed breast milk concentrations.

Because of limited data on serum and breast milk perchlorate concentrations in people and the uncertainties with the PBPK models as they relate to fetal and neonatal life stages, as noted above[14], MassDEP has concluded that it is not possible at this time to derive meaningful quantitative estimates of infant perchlorate exposures from breast milk that would result from maternal drinking water exposures. However, the experimental data that indicates perchlorate is concentrated into milk from the serum suggests that, in order to keep the breast milk concentration of perchlorate below 1.4 µg/L, the perchlorate concentration in the drinking water of the nursing mother may need to be below this concentration[15].

Although, as noted throughout this discussion, there are significant data gaps that preclude robust quantitative assessment of this exposure pathway, the qualitative data emphasize its potential significance relative to exposures and risks to those considered to be among the most sensitive to perchlorate toxicity. This argues for a conservative, health protective approach. As previously discussed, uncertainty regarding perchlorate's inhibition of iodide transport into milk, which could increase neonatal sensitivity to perchlorate thyroid effects, is one of several uncertainties that support MassDEP's use of a database deficiency uncertainty factor. The levels of perchlorate detected in breast milk also support the use of a conservative relative source apportionment factor for maternal drinking water exposures to perchlorate.

3.3 RfDS AND ASSOCIATED DRINKING WATER LIMITS.

In light of the issues discussed above, MassDEP scientists in consultation with the Advisory Committee on Heath Effects concluded that a weight of the evidence approach should continue to be used to determine the most appropriate RfD value and corresponding drinking water value. Thus, both the human and animal data were considered by MassDEP in its assessment. In part based on the NAS report, MassDEP is now placing more weight on the human data.

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[14] At the 2/05 meeting of the MA DEP-DPH Advisory Committee on Health Effects, one participating NAS Committee member noted that premature infants constitute an additional group at risk. To our knowledge, PBPK models addressing perchlorate exposures to premature infants have not been developed.

[15] Note: Although the following calculations are very uncertain because of limited data, they support a health-protective approach to the selection of the uncertainty factors used to derive a final RfD and exposure apportionments used to derive any drinking water limit for perchlorate for lactating women. Serum perchlorate concentrations in individuals (9 men) exposed to approximately 0.14 mg/kg-day of perchlorate in drinking water averaged 0.61 mg/L (Lawrence et al. 2000). Based on this data and using a linear extrapolation, exposures to perchlorate at the NAS lower RfD of 2.3×10^{-4} mg/kg-day would be expected to result in a serum concentration of approximately 0.001 mg/L (note: the PBPK models suggest that proportionally higher serum concentrations may result at lower doses, so this value may be an underestimate of the serum concentration). Assuming that the 10-fold serum to breast milk concentration factor observed in rodents applies to humans as well, this would imply a breast milk perchlorate concentration of 10 µg/L. This value is 7-fold higher than the acceptable breast milk target concentration of 1.4 µg/L, which can be derived based on the lower of the two NAS RfDs, and 23 times higher than that which can be derived based on MA DEP's RfD. As the adult drinking water limit associated with the NAS lower value is 1.6 µg/L, the final drinking water limit for lactating women would, in this scenario, be well below 1 µg/L. The final drinking water limit for lactating mothers would have to be below 1 µg/L even on the basis of the higher NAS RfD, which is associated with an adult drinking water limit of 4.9 µg/L based on standard exposure parameters that do not account for breast milk. These preliminary calculations are by no means definitive but do suggest a need for further research to better delineate the relationship between maternal perchlorate exposures, levels in breast milk and exposures to the nursing infant.

MassDEP and its MassDEP/DPH Advisory Committee on Health Effects, noting that the statistical power of the Greer study was such that a 40% inhibition of iodide uptake would have had to occur to be statistically detectable with a reasonable level of confidence, have concluded that an UF of 30 is the minimum that should be used with this data. One Committee member supported this value over others. Based on the full range of uncertainties involved, including data which indicates that perchlorate may be concentrated into breast milk, the remaining members of the Advisory Committee on Health Effects recommended that a total UF of at least 100 should be applied. Some members indicated that a higher UF of 300 could be supported. Application of UFs of 100 or 300 to the Greer data yields RfDs of 7×10^{-5} mg/kg-day and 2.3×10^{-5} mg/kg-day, respectively. As discussed in preceding sections, the animal data can support RfDs of 2.8×10^{-5} and 8.5×10^{-5} mg/kg-day. These values are in the same range as those that can be derived from the human data.

These RfD's along with the associated drinking water values are summarized in Table 6. The higher of the two NAS RfDs is footnoted in the Table for comparative purposes although MassDEP and the Advisory Committee on Health Effects unanimously concluded this value does not adequately account for the uncertainties in the data, including the breast milk exposure pathway[16].

Based on the weight of the evidence as discussed in this report, MassDEP has concluded that the RfD value of 7×10^{-5} mg/kg-day, based on the Greer study data and a composite uncertainty factor of 100, provides a scientifically defensible basis for evaluating exposures. This value is associated with a drinking water limit of 0.49 µg/L (adults) and 0.44 µg/L (formula-fed infants). Based on an RfD of 2.3×10^{-4} mg/kg-day, the highest value supported by the DEP/DPH Advisory Committee on Health Effects (one member) and the lowest value supported by the NAS Committee (one member) a drinking water value of 1.6 µg/L (adults) or 1.4 µg/L (formula-fed infants) would be supported.[17]

As noted earlier, upon completion of the above document and during the internal review period, a few new perchlorate studies and assessments were published and/or made available. For completeness, MassDEP reviewed these studies in light of their importance towards setting a perchlorate RfD and also received input from the MassDEP/DPH Advisory Committee on Health Effects. The results of this detailed review are presented in a separate Addendum along with conclusions that the newer studies do not present information sufficient to warrant altering MassDEP's proposed RfD value.

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[16] To reiterate, breast milk exposure is an emerging issue that was not considered by NAS. Data released in February 2005, and thus not available to the NAS Committee, indicate that perchlorate is prevalent in breast milk at concentrations that frequently exceed values that would be appropriate for the neonate.

[17] MassDEP notes that if an adjustment is conducted using standard default values for the child body weight (10 kg) and child drinking water consumption (1 L/day), resulting drinking water limits are 0.046 ppb and 0.14 ppb based on total uncertainty factors of 300 and 100, respectively.

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Table 1. Comparative Summary of Human Perchlorate Exposure Studies.

*not peer reviewed; Key: O – no effect observed; ↓ - decrease in value of variable; NR – not reported; ** calculated by MassDEP assuming 70 kg body weight

Study	N	Daily Dose mg	Mg/kg/d	Duration (wks) 0 2 4 6 8 // 12 24 28	Effects RAIU	Total Serum T4	Free Serum T4	Total Serum T3	Free Serum T3	TSH	other
Brabant et al., 1992	5♂	0.2	0.003** iodide	----------|	-	O		O			O (Thy. vol)
		910	13** perchl.	|----------|	-	↓			O	↓	↓ (Thy I^- content) ↓ Serum thyroglobulin
Brabant pers. comm. 1994 (cited in U.S. EPA, 2002)*	NR	NR	12	----------.>4 wks	-	-	-	-	-	O	↑ Thyroid volume
Lawrence et al., 2000	9♂	10	0.1**	-------|……| follow-up	↓ + post recovery		O	O		O	O urine Iodine
Lawrence et al., 2001*	8♂	3	0.04**	-------|……| follow-up	↓ NS + post exp. ↑	O	-	O	-	O	-
Greer et al., 2002	7	NR	0.007	--------|……..| +15d follow-up	O	O	O	O		O	-
	10	NR	0.02	--------|……..| +15d follow-up	↓	O	O	O		O	
	10	NR	0.1	--------|……..| +15d follow-up	↓ + recov.	O	O	O		O	
	10	NR	0.5	--------|……..| +15d follow-up	↓+ recov	O	O	O		↓+ Recov.	
Braverman et al., 2004*	4	0	0	----------|……| post exp.	O	O		O		O	
	5	0.5	0.007**	---------- ----------|……| post exp.	O	O		O		O	
	4	3	0.04**	---------- ------|……| post exp.	O	O		O		O	

DOSES:	0	0.007	0.02	0.04	0.1	0.5	13
Σn		12	10	12	19	10	5

Table 2. Factors for Evaluating Evidence Regarding Identification and Characterization of Susceptible Subpopulations. Source: U.S. Environmental Protection Agency , 2002c

Factor	Increased weight	Decreased weight
Timing (life stage) - response relationship	Effects occur at greater magnitude at one or more life stage(s)	No difference in effects at different life stage(s)
Type of effect	Different types of effects in specific subpopulations	Same effect(s) across all potential subpopulations
Dose-response relationship	Effect occurs at lower exposures in one or more subpopulation(s)	No evidence for differential dose-response across different subpopulations
Latency of effect	Latency to observed effect different in specific subpopulations	No difference between subpopulations in latency to effect
Seriousness/ reversibility of effects	Effects different in seriousness or degree of reversibility in specific subpopulations and/or differences in later consequence of an initially reversible effect	No differences between subpopulations in seriousness and/or reversibility of effects, or in later consequences of an initially reversible effect

[a] *Subpopulations may be defined by gender, individuals at different life stages (fetus, child, adult, elderly),* differences in genetic polymorphisms, and/or pre-existing diseases or conditions that may result in differential sensitivity to adverse effects from exposure to a specific toxic agent.

Table 3. Perchlorate Dose Levels Associated with Significant Changes in Thyroid and Pituitary Hormone Levels at Different Life Stages

Generation	T3 LOAEL mg/kg-day	T4 LOAEL mg/kg-day	TSH LOAEL mg/kg-day	Brain morphometry (corpus callosum, striatum, cerebellum) LOAEL mg/kg-day	References
GD21 (Dams)		0.01 0.004 (BMDL)	0.01		Argus Research Laboratories, Inc., 2001
GD21 (PUPS)	0.01				Argus Research Laboratories, Inc., 2001
PND4, PND9	0.01				Argus Research Laboratories, Inc., 2001
PND21		0.01 (LOAEL) 2.86×10^{-7} (BMDL)	0.01 (female)	0.01	Argus Research Laboratories, Inc., 2001

Note: Dose values in the table are for potassium perchlorate, which translates into 0.0085 mg/kg-day of perchlorate

Table 4. Qualitative Consistency of Effects of Perchlorate on Thyroid and Pituitary Serum Hormones* (Table reproduced from U.S. Environmental Protection Agency, 2003)

Study	Time Point	T4	T3	TSH
Rat 14 Day (Caldwell et al., 1995)	14-Day	↓	↓	↑
Rat Subchronic (Springborn, 1998)	14-Day	↓	↓	↑
	90-Day	↓	↓	↑
Rat Neurodevelopmental (Argus, 1998a)	PND5	↓	↓	↑
Rat Argus"Effect Study" (Argus, 2001)	Dams - GD21	↓	↓	↑
	Dams - PND10	↓	↓	↑
	Dams - PND22	↓	↓	↑
	F1 - GD22	↓	↓	↑
	F1 - PND5	↓	↓	↑
	F1 - PND10	↓	↓	↑
	F1 - PND22	↓	↓	↑
Rat 2-Generation Study	P0 Males	↓	--	↑
	P0 Female	--	--	--
	P1 PND21	↓	--	↓
Mouse Subchronic	14-Day	↓	↓	↑
	90-Day	↓	↓	NA
Rabbit Developmental (Argus, 1998b)	Gestation Day 28	↓	↓	↑

*see Tables 5-2and 5-4 of the 2002 ERD provided herein in Appendix 4B as Tables 4B-1 and 4B-2 for details.
NOAEL and LOAEL estimates were determined by Agency ANOVA for the individual studies.
NA = not available

Table 5. Effects of Perchlorate on Rat Pituitary and Thyroid Hormone Levels Relative to Controls (Argus, 2001)

PND 21 dams	0.01 mg/kg-day (ClO_4^- dose)	0.1 (mg/kg-day (ClO_4^- dose)	1 (mg/kg-day (ClO_4^- dose)	30 (mg/kg-day (ClO_4^- dose)
% Decrease in T4 levels	11	45	48	54
% increase in TSH levels	35	50	64	146

Table 6. Range of Possible RfDs and Associated Drinking Water Values Derived from Human and Animal Studies with MassDEP and NAS Assigned Uncertainty Factors

STUDY		Total Uncertainty Factor Applied			
		UF 300[1]	UF 100[2]	NAS UF 30[3]	Notes
Greer study	**RfD mg/kg-day**	2.3×10^{-5}	7.0×10^{-5}	2.3×10^{-4}	-
	a) Health Based Adult Drinking Water Value (µg/L or ppb)	0.161	**0.490**	1.610	For 70 kg adult; 2 L/day water consumption; 20% source apportionment factor
	b) Formula-fed Infant Health Based Drinking Water Value	0.137	**0.438**	1.373	For 4 kg infant; 0.64 L/day formula consumption; 100% source apportionment factor
Argus study	**RfD mg/kg-day**	2.8×10^{-5}	8.5×10^{-5}	NA	-
	a) Health Based Adult Drinking Water Value (µg/L or ppb)	0.196	0.595	NA	For 70 kg adult; 2 L/day water consumption; 20% source apportionment factor
	b) Formula-fed Infant Health Based Drinking Water Value	0.167	0.507	NA	For 4 kg infant; 0.64 L/day formula consumption; 100% source apportionment factor

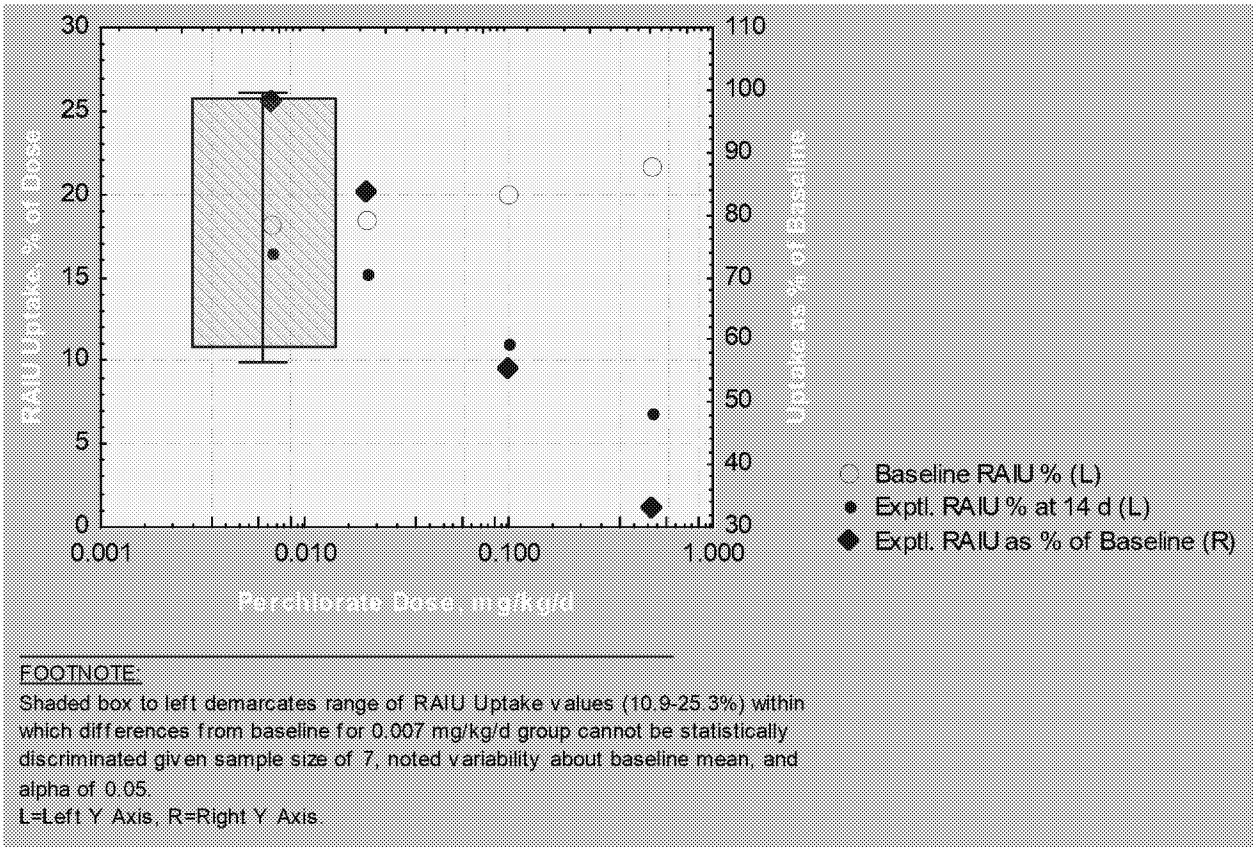
Table notes:

1 RfD value that would result from use of an UF of 300, an option that some members of the MADEP/DPH Advisory Committee on Health Effects indicated could be supported by the data.

2 Final MassDEP proposed RfD value, unamimously supported by MADEP/DPH Advisory Committee on Health Effects.

3 RfD value that one member of the DEP/DPH Advisory Committee on Health Effects and one member of the NAS Committee supported.

4 If the RfD, proposed by the NAS Committee (based on the Greer study) and adopted by USEPA were used, the associated drinking water limits for adults and infants would be approximately 4.8 µg/L and 4.2 µg/L, respectively.



FOOTNOTE:
Shaded box to left demarcates range of RAIU Uptake values (10.9-25.3%) within which differences from baseline for 0.007 mg/kg/d group cannot be statistically discriminated given sample size of 7, noted variability about baseline mean, and alpha of 0.05.
L=Left Y Axis, R=Right Y Axis.

Figure 1. Iodide Uptake Data from Greer et al 2002. Means with Low Dose Group Baseline Std. Dev.

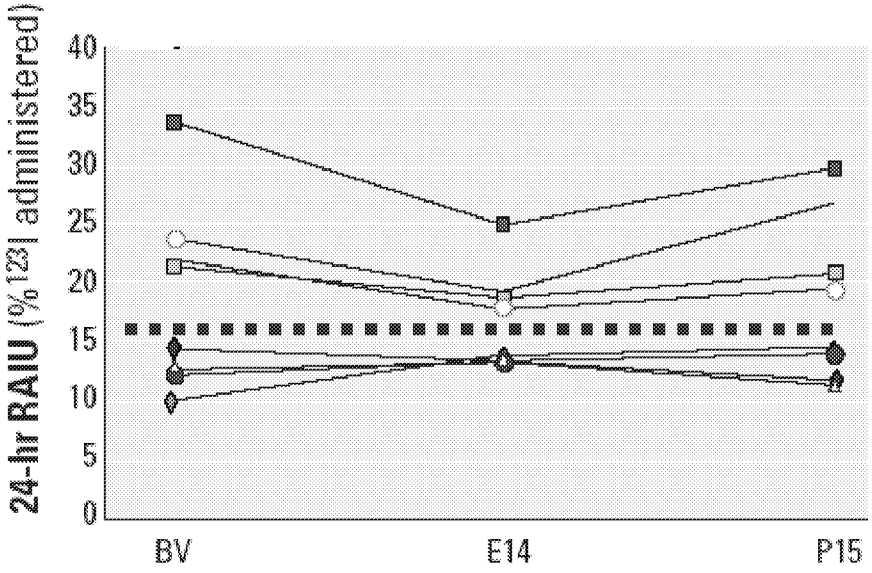


Figure 2. Individual Baseline (BV), 14 day Exposure (E14) and 15 day Post-Exposure (P15) 24-hour RAIU Responses for 0.007 mg/kg/d Dose Group. Dotted Line Added to Emphasize Differences Between Individuals Based on Baseline RAIU Level (Adapted From: Greer et al. 2002).

APPENDICES

Appendix A

The Rat as an Animal Model for Perchlorate Toxicity

The NAS Committee stated that the rat is more sensitive than humans to perchlorate disruption of thyroid function and thus concluded that the rat was not a good model to study perchlorate toxicity. The NAS noted that rats exhibit:

(a) higher thyroid hormone turnover rate and lower thyroid storage capacity than observed in humans;
(b) lower thyroid hormone levels in normal pregnant rats compared to normal pregnant women; and,
(c) delayed thyroid gland development in rat fetuses compared to human fetuses.

These issues are briefly discussed below:

Thyroid Hormone Turnover Rate and Thyroid Storage Capacity

Greer et al. (2002) pointed out that: (a) the rat thyroid is much more responsive to perturbation of iodine metabolism, leading to decreased hormone formation; (b) if thyroid hormone synthesis is prevented, the rat thyroid contains only enough hormone to last a few days, while the iodide sufficient healthy human thyroid has enough thyroid to last several months; and (c) the rat thyroid is rapidly upregulated in response to multiple treatments with perchlorate, a phenomenon not observed in humans treated for 14 days with perchlorate. These differences were also discussed by the National Academy of Sciences (2005). In the comparisons made between rats and humans above, it is not clear if the rat is expected to have thyroid hormone storage capacity and thyroid upregulation time frames exactly similarly to humans, or whether there are known human-equivalent time frames for these parameters that the rat failed to meet.

These conclusions on rat versus human sensitivity to perchlorate-induced thyroid function disruption seem to contrast with the general physiological literature on inter-species scaling. It is well known in physiology that physical dimensions, and physiological and biochemical functions in different species are functions of metabolic rate which in turn relates to various exponents of body weight (Kleiber, 1947; Adolph, 1949; Krasovskij, 1976[18]). This biological regularity provides a basis for the use of small animals as models for human toxicological and pharmacological studies and for interspecies extrapolation, provided appropriate adjustment is made.

[18] Intake of water, urine output, urea clearance, creatinine clearance, Diodrast clearance, hippurate clearance, oxygen consumption-basal, heartbeat duration, breath duration, ventilation, tidal volume, gut beat duration, total nitrogen output, endogenous nitrogen output, creatinine nitrogen output, sulfur output, oxygen consumption in liver slices, hemoglobin weight, myoglobin weight, cytochrome weight, nephron number, renal corpuscle diameter, and weight of heart, kidneys, lungs, liver, thyroid, adrenals, pituitary, stomach, intestine, and blood (Adolph , 1949); duration of pregnancy, number simultaneously born offspring, latent period of tumor formation, nerve and muscle cell dimension, maturation time of bone marrow, cellular elements, duration of erythrocyte life (Krasovskij, 1976).

Much of the fundamental work on this topic came from studies of metabolism in different sized organisms (Kleiber,1947). The work of others expanded to other physiological and morphometric variables relationships with size. Adolph (1949) reported over 30 mammalian biological parameters[17] to be mathematical functions of body weight. Adolph's work was verified by Krasovskij (1976). This author also established linear relationships among 100 mammalian biological parameters and body weight and described this relationship as "biological regularity". Krasovskij expressed this "biological regularity" by an allometric exponential equation of the form $x = ay^b$ or by a linear-line equation $\log x = \log a + b \log y$. When the biological parameter is standardized by dividing by body weight, the relationship becomes described by a negative exponential curve, or by a straight line with negative slope if both the biological variable and weight are log transformed. This weight standardization is the basis for the well- recognized rule that smaller organisms have higher metabolic rates per unit of body mass than larger organisms, whereas their absolute metabolic rates are of course less than those of much larger sized organisms. The generalized results from two classic interspecies sensitivity studies (Pinkel, 1958; Freidreich et al.,1966) found that smaller animals were less sensitive (i.e, require greater effective doses to produce the same effect than in humans) to chemical toxicity than larger ones when compared on a mg/kg body weight basis: an important point vis-à-vis perchlorate. Concomitantly, smaller animals like rats have greater weight-specific physiological parameter rates than humans.

These generalizations relate directly to thyroid functioning. Basal metabolic rate (BMR) was historically used as a clinical tool for determining thyroid status in humans. The production and secretion of thyroid hormone is related to body mass with the same exponent of 0.75 that holds for BMR (Hulbert et al., 2004). From this relationship, one can infer that the rates of these thyroid hormone processes are greater in rats (and likely other small animals) than in larger animals when expressed on a body weight basis. There does not, however, seem to be any significant relationship of either total or free thyroid hormone concentrations in the plasma of animals to weight (Hulbert et al., 2004). This finding for thyroid hormone production rate is entirely consistent with the classic metabolic-size and dose-size paradigm, yet it is a high turnover rate of thyroid hormones in rats that was cited by National Academy of Science (2005) as one reason for characterizing rats as being potentially more sensitive to perchlorate-induced disruption of thyroid function than humans. The existence of these two apparently contrasting views of thyroid function sensitivity in rats compared to humans suggests this issue deserves closer scrutiny and that it may be premature to dismiss rats as models for human perchlorate toxicity because of their greater responsiveness or sensitivity than humans. The situation that exists is what is expected based upon classic interspecies scaling relationships.

Thyroid and Pituitary Hormone Levels in Pregnant Women and Pregnant Rats

In humans, normal pregnancy is accompanied by a rise in serum levels of T4 and T3. However due to an increase in T4-binding globulin, the free T4 and T3 levels decrease during pregnancy (Glinoer et al., 1990). In contrast to findings in humans, serum T4 and T3 levels in the rat during 17 to 22 days of gestation are decreased, leading to reduced concentration of T4 and T3 in tissues, except for T3 in the brain (Calvo et al., 1990). If this late gestation phenomenon in the rat also occurs during other stages of pregnancy, the pregnant rat can serve as a good model to study the effects of perchlorate in marginally iodine sufficient and subclinically hypothyroid women

who would be expected to exhibit comparatively lower levels of thyroid hormones. Hollowell et al. (2002) estimated that 4.6 percent of the United States population has hypothyroidism (0.3 percent clinical and 4.3 percent subclinical). Kung et al. (2000) studied marginally iodine sufficient pregnant women and found that pregnancy in these women decreased T4 and T3 levels (Table 1), as was observed in pregnant rats by Calvo et al. (1990) and Versloot et al. (1994).

The usefulness of the rat as a model for pregnant women cannot be ruled out. Pregnancy itself puts pressure on the thyroid gland. Among other changes in thyroid function, pregnancy increases the demand for iodine due to pregnancy-associated iodide clearance by the kidney (because of increased glomerular filtration rate), and transfer of maternal iodide to the fetus (Glineor, 1990). Any decrease in iodide uptake inhibition caused by perchlorate could create a negative iodide balance at any stage in pregnancy, causing a decrease in thyroid hormone synthesis.

Delayed Rat Fetal Thyroid Gland Development

Much of the knowledge regarding the maturation of thyroid function in the fetus and neonate is derived from studies in rats. The rat is a good model to study human thyroid gland development and differs primarily in the timing of events. The thyroid gland of the rat fetus starts to function between days 17 and 18 of gestation (Morreale de Escobar et al., 1985). Because of this late development of the thyroid gland, the rat fetus depends entirely on the mother's thyroid hormone during the greater part of *in utero* development. The rat fetus may thus provide an animal model to study the congenitally hypothyroid human fetus. Congenital hypothyroidism is one of the commonest causes of mental retardation in humans and its causes and prevalence are presented in Table 2. Since the rat fetus has some contribution of its own thyroid hormone during the last stages of its *in utero* development, this fact should be taken into consideration when extrapolating data from the animals to humans. The human hypothyroid fetus may be more sensitive to perchlorate because of a lack of any other thyroid hormone sources except its mother's, throughout gestation.

In conclusion, data on perchlorate toxicity derived from studies on the rat should not be completely discounted. In fact, the rat may be a reasonable model to study the toxicity of perchlorate during sensitive human lifestages such as the pregnant woman and the congenitally hypothyroid fetus. MassDEP is therefore continuing to use the animal bioassay data in its analysis but as supporting information. In acknowledgement of the uncertainty about the sensitivity of the rat model in comparison to healthy adults, MassDEP has considered alternative uncertainty factor adjustments for the animal data.

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Table 1. Changes of Thyroid Function Tests, Thyroidal Volume and Urinary Iodine Level of Marginally Iodine sufficient Women During and After Pregnancy (Kung et al, 2000)

Parameter	First trimester	Second trimester	Third trimester	Postpartum 6 weeks	Postpartum 3 months
Total T4 (nmol/L)	154	126*	125*	89**	92**
Free T3 (pmol/L)	3.9	3.4*	3.3*	4.0	4.0
Free T4 (pmol/L)	13.4	11.9*	11.7*	14.5	14.4
TSH (mIU/L)	0.49	0.96*	0.95**	1.15**	1.14**
Urine iodine μgl /L	10.6	11.5*	12.4*	10.5	10
Thyroid volume	9.5	10.3*	11.2*	11.0*	10.6*

Results are median, * $p < 0.05$, ** $p < 0.01$, vs first trimester

Table 2. Thyroid Disorders And Their Approximate Prevalences In The Human Neonatal Period (Post et al. 1996) Table adopted from US EPA (2002).

Thyroid Dysgenesis	1:4000
Agenesis	
Hypogenesis	
Ectopia	
Thyroid Dyshormonogenesis	1:30,000
TSH unresponsiveness	
Iodide trapping defect	
Organification defect	
Defect in thyroglobulin	
Iodotyrosine deiodinase deficiency	
Hypothalamic-Pituitary Hypothyroidism	1:100,000
Hypothalamic-pituitary anomaly	
Panhypopituitarism	
Isolated TSH deficiency	
Thyroid hormone resistance	
Transient Hypothyroidism	1:40,000
Drug induced	
Maternal antibody induced	
Idiopathic	

Appendix B

Brain Morphometric Data from Animal Studies

The NAS (2005) document extensively discussed the Argus Research Laboratories (1998, 2001) brain morphometric analyses, and pointed out that there was no dose-effect relationship and no consistent effect across age and sex except for the corpus callosum which increased in size at the highest dose tested (10 mg/kg/day) at different life stages. The NAS also noted that the Argus (2001) study showed significant increase in the corpus callosum across life stages at all doses except the highest dose tested (30 mg/kg/day). The NAS was concerned about the lack of a dose-effect relationship after comparing the Argus (1998) and (2001) studies. In the Argus (1998) study the thickness of the corpus callosum was increased only at 10 mg/kg/day and not at 3 mg/kg/day. In contrast, the corpus callosum size was increased at doses ranging from 0.01 to 1 mg/kg/day, but not at 30 mg/kg/day in the Argus (2001) study.

However, the NAS did not consider the dosing protocols (duration of exposure and dose spacing) used in the two studies. In the Argus (1998) study, female rats were exposed to perchlorate beginning on gestation day 0, while in the Argus (2001) study, female rates were exposed 2 weeks before cohabitation with male rats. In the Argus (2001) study, female rats were made hypothyroid before pregnancy while the female rats in the Argus (1998) study, were euthyroid at pregnancy. Previous studies by Springborn Laboratories (1998) have shown that rats treated with perchlorate for two weeks had significant changes in thyroid and pituitary hormone levels at 0.01 mg/kg/day, which is the dose that resulted in changes in brain morphometry in the Argus (2001) study. These observations suggest that the two studies should only be qualitatively compared. Lack of dose-response concordance between the two studies should not be a valid reason to discredit the results of the studies.

The NAS (2005) document also discussed other issues surrounding the brain morphometry data including:

(a) method of brain tissue fixation and time since fixation before sectioning and slicing of tissues;
(b) variation in plane of section;
(c) differences in plane of sectioning across animals;
(d) coronal versus sagittal sectioning of the corpus callosum; and
(e) lack of non-blinded morphometric measurements.

The NAS report indicated that the Committee did not think issues (a) and (b) above were of concern in the overall evaluation of the brain morphometry data. Regarding issue (c), the NAS stated that the US EPA resectioned and reanalyzed brain tissues from PND 22 pups, which helped to dispel some of the concerns that have been raised about systematic differences in the plane of section among treatment groups. However, the NAS was concerned that the reanalysis of the brain tissues has contributed to the inconsistencies in the data set because the thickness of the striatum were decreased in the 2001 brain section and increased in the 2003 brain section from the same pups. Like the NAS, MassDEP also observed these inconsistencies while

reviewing the US EPA (2003) document in 2004. The data in the 2002 and 2003 EPA documents on the corpus callosum were consistent while the data on the striatum were inconsistent. MassDEP previously contacted US EPA scientists involved in the perchlorate toxicity assessment for clarification of the divergent results of the striatal data set. Dr. Geller (personal communication) explained that the 2002 analysis was based on the combined male and female data, while the 2003 analysis was based only on male data. As seen in Table 1, perchlorate dosing was associated with a decrease in striatal size in females and an increase in males. It is not clear why the male and female striatal data were combined for analysis when there is clear evidence of treatment and sex interaction.

Of note is the observation that the effects of perchlorate on the striatum are reproducible at multiple doses and multiple life-stages, as it is with the corpus callosum. Wahlsten (2002) also reproduced the results on the striatum. Moreover, the coronal sectioning of this region of the brain is said to be not as controversial as it is with the corpus callosum. Issues (d) and (e) are of concern, but these issues may not be sufficient grounds to discount the brain morphometry data.

While MassDEP is still concerned with some methodological problems of the brain morphometry data, the consistent observation of perchlorate-related effects in the corpus callosum and the striatum observed in two separate studies at different life stages, and the concordant morphometric measurements performed by two separate pathology laboratories cannot be ignored. The data suggest that perchlorate may change brain morphometry in rats exposed *in utero* and postnatally. Moreover, the NAS (2005) also stated that the corpus callosum thickness was increased at multiple doses and at several stages of development (PND10-12, PND22, PND 82-85) in two studies and is suggestive of a relationship between perchlorate exposure and altered neurodevelopment. The NAS also reviewed several studies to establish biological plausibility of the effects of perchlorate on the corpus callosum, and concluded that although not widely recognized as a classic marker of neonatal hypothyroidism, increased thickness of the corpus callosum appears to be a biologically plausible effect. Thus MassDEP views the brain morphometry data as qualitatively informative but is no longer relying on this data to quantitatively assess perchlorate risks.

REFERENCES

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Argus Research Laboratories. 2001. Hormone, Thyroid and Neurohistological Effects of Oral (Drinking Water) Exposure to Ammonium Perchlorate in Pregnant and Lactating Rats and in Fetuses and Nursing Pups Exposed to Ammonium Perchlorate During Gestation or Via Material Milk.Argus Research Laboratories, Inc. (as cited in U.S. EPA, 2002). Horsham, PA.

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Springborn Laboratories, I. 1998. A 90-Day Drinking Water Toxicity Study in Rats With Ammonium Perchlorate.Springborn Laboratories, Inc., Health and Environmental Sciences. Spencerville, OH.

Wahlsten, D. 2002. Perchlorate Effects on Rat Brain Morphometry: A Critical Evaluation. Submitted to Eastern Research Group, Inc. for the U.S. EPA /ORD Peer Review Workshop-Perchlorate Environmental Contamination: Toxicological Review and Risk Characterization, March 5-6,Sacramento, CA. February 19. [Online]. Available: http://www.perchloratesymposium.com/docs/Wahlsten2002.pdf

Table 1. Summary of Morphometric Findings in Rat Pups Exposed to Perchlorate

Brain regions	Argus 1998 PND10 -12 LOAEL	Argus 1998 PND62 – 65 LOAEL	Argus 2001 PND 10 LOAEL	Argus 2001 PND22 LOAEL	EPA 2003 PND 22 LOAEL
Frontal Cortex	No change	↑ 10 (m)	↑ 1.0	0.1 ↑	Not measured
Parietal cortex	No change	No change	↑ 1.0	No change	Not measured
Striatum	↓ *3.0 (f)	↑ 10 (m)	↑ 1. 0 (m) ↓0.1(f)	↓ 0.01 (m +f)	↑ 0.01 (m)
Corpus callosum	↑ 10	↑ 10 (m)	↑ 0.1 (m)	↑ 0.01	↑ 0.01
Hippocampus gyrus	↓ 3.0	No change	No change	No change	Not measured
Dental gyrus	Not measured	Not measured	No change	No change	Not measured
CA1 portion	Not measured	Not measured	↓1.0 (f) ↑(m)	No change	Not measured
CA3 portion	Not measured	Not measured	No change	↓ 0.1	Not measured
External germinal layer of cerebellum	Not measured	Not measured	↓ 1.0	No change	Not measured
Anterior/posterior cerebellum	↑ 3.0	No change	No change	↑ 0.01	Not measured

↑ = Increase in size; ↓ = decrease in size; m = male; f = female
* Numbers in the table are doses in mg/kg/day at which effect was noted

Appendix C

Modest Thyroid Hormone Decrement in Pregnant Women and Impaired Neurodevelopment in the Offspring

Haddow et al.(1999) measured thyrotropin (TSH) levels in stored serum samples collected from 25,216 pregnant women (during the second trimester) in Maine between January 1987 and March 1990. They then located 47 women with serum thyrotropin concentrations at or above the 99.7th percentile of the values for all the pregnant women, and 15 women with values between the 98th and 99.6th percentile, inclusive, in combination with low serum T4 and free T4 levels. The 7-9 year old children of these women were further investigated, none with hypothyroidism at birth The authors then conducted 15 tests on the children of these women as well as controls, relating to intelligence, attention, language, reading ability, school attainments, and visual-motor performance. The staff giving the tests did not know whether the children's mothers were women with hypothyroidism or control women. To establish a suitable control group, the authors selected 124 children born to euthyroid mothers, matched for various items such as the women's age at delivery, gestational age at blood sampling, and duration of serum storage. A scoring system was used to check for possible differences in socioeconomic status of the families (number of years of education and occupation of both parents). They found that the children of the 62 women with high serum thyrotropin concentrations performed slightly less well on all 15 tests and scored, on average, 4 IQ points lower compared to controls. Of the 62 women with thyroid deficiency, 48 were not treated for hypothyroidism during pregnancy. The average IQ score of their children was 7 points lower than the controls. Haddow *et al.* (1999) concluded that that even mild and probably asymptomatic hypothyroidism in pregnant women could adversely affect the neuropsychological performance of their offspring. From the Haddow et al. study it can be seen that T4 decreases in the pregnant mother as low as 30% may be associated with neuropsychological deficits in offspring, which is in the range of the T4 decreases observed in the critical Argus Research Laboratories (2001) study (Table 1).

In a follow-up study, Klein et al. (2001) studied serum TSH concentrations of pregnant mothers at 17 weeks of gestation and performed the standard neuropsychological testing in the offspring at mean age of 8. These authors found that the severity of neuropsychological deficits in the offspring was associated with maternal hypothyroidism. The hormonal status of subjects in this study might not be different from those in the Haddow et al. (1999) study, as both studies appear to have used subjects from the same sample pool. The results of the Klein et al. study support a causal association of low thyroid hormone level in the pregnant woman and poor neuropsychological development in the progeny.

Modest and Transient Thyroid Hormone Decrement in Pregnant Rat and Altered Brain Structure in Offspring

Auso et al. (2004) designed an experiment where mild transient hypothyroidism was induced in pregnant rats by treating these rats with a known goitrogen (2-mercapto-1-methyl-imidazole) for

only 3 days, from gestation day 12 to gestation day 15. Maternal thyroid hormones transiently decreased by about 30% in this study, without clinical signs of hypothyroidism. The pups born to treated dams were tested for audiogenic seizure susceptibility 39 day after birth and killed after postnatal day 40 to examine brain structure. The structure and distribution of the cortex and hippocampus were altered in 83% of the pups. Pups born to the treated dams (52%) also responded to an acoustic stimulus, followed in some by seizures. The authors concluded that even mild hypothyroxinemia should be prevented before and during pregnancy. Such study designs could in the future help identify the threshold for thyroid hormone decreases associated with brain structure alterations and other thyroid hormone deficiency-related effects. Until then, the 11% (Table 1) decrease in T4 and the 35% increase in TSH observed in the Argus (2001) study should remain of concern. The dose of perchlorate (0.01 mg/kg/day) associated with these effects provides a reasonable point of departure for deriving an animal data based RfD for perchlorate.

REFERENCES

Argus Research Laboratories. 2001. Hormone, Thyroid and Neurohistological Effects of Oral (Drinking Water) Exposure to Ammonium Perchlorate in Pregnant and Lactating Rats and in Fetuses and Nursing Pups Exposed to Ammonium Perchlorate During Gestation or Via Material Milk.Argus Research Laboratories, Inc. (as cited in U.S. EPA, 2002). Horsham, PA.

Auso, E., Lavado-Autric, R., Cuevas, E., Del Rey, F. E., Morreale De Escobar, G., and Berbel, P. 2004. A moderate and transient deficiency of maternal thyroid function at the beginning of fetal neocorticogenesis alters neuronal migration. Endocrinology. 145. pp.4037-47.

Haddow, J. E., Palomaki, G. E., Allan, W. C., Williams, J. R., Knight, G. J., Gagnon, J., O'Heir, C. E., Mitchell, M. L., Hermos, R. J., Waisbren, S. E., Faix, J. D., and Klein, R. Z. 1999. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med. 341. pp.549-55.

Klein, R. Z., Sargent, J. D., Larsen, P. R., Waisbren, S. E., Haddow, J. E., and Mitchell, M. L. 2001. Relation of severity of maternal hypothyroidism to cognitive development of offspring. J Med Screen. 8. pp.18-20.

Table 1. Effects of Perchlorate on Rat Pituitary and Thyroid Hormone Levels Relative to Controls (Argus, 2001)

PND 21 dams	0.01 mg/kg-day (ClO_4^-)	0.1 mg/kg-day (ClO_4^- dose)	1 mg/kg-day (ClO_4^- dose)	30 mg/kg-day (ClO_4^-) dose
% Decrease in T4 levels	11	45	48	54
% increase in TSH levels	35	50	64	146

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 5/13/2020 8:24:42 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]; Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]
CC: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Flaharty, Stephanie [Flaharty.Stephanie@epa.gov]
Subject: RE: FOR REVIEW: draft perchlorate action and transmittal memos
Attachments: Transmittal Memo JM to DR 5-13-20 v1.docx; Perchlorate Action Memo 5-13-2020 .docx

Lisa:
Attached please find my suggested edits to the Perchlorate transmittal memo and action memo. I modified the memos to reflect our status of submission to OMB for Interagency review.
I am copying Stephanie so that she may provide any additional edits to assure consistency with Agency templates.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Wednesday, May 06, 2020 3:51 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FOR REVIEW: draft perchlorate action and transmittal memos

DRAFT DELIVERABLE
Hi Eric,
For you review are the draft memos to accompany the perchlorate final action. Please let us know if you have question, concerns or need more information.
Thanks,
Lisa

Message

From: Flaharty, Stephanie [Flaharty.Stephanie@epa.gov]
Sent: 5/22/2019 12:37:42 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
CC: Huff, Lisa [Huff.Lisa@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Tiago, Joseph [Tiago.Joseph@epa.gov]
Subject: Current Perchlorate Memos
Attachments: Transmittal Memo EB to JM 5-20-19 SHQ.SF.docx; Transmittal Memo JM to DR 5-20-19 SHQ.SF.docx; Perchlorate Action Memo 5-21-19.docx

Sam,

Eric has signed and initialed the transmittal memos. Note, the Action Memorandum still needs the OMB language stating the completion of its review.

Thanks,
Steph

From: Burneson, Eric
Sent: Wednesday, May 22, 2019 8:19 AM
To: Lousberg, Macara <Lousberg.Macara@epa.gov>; Evalenko, Sandy <Evalenko.Sandy@epa.gov>; Flaharty, Stephanie <Flaharty.Stephanie@epa.gov>
Subject: FW: For your review: Perchlorate - pass back language

FYI: Awaiting feedback from Dave

From: Burneson, Eric
Sent: Tuesday, May 21, 2019 7:36 PM
To: Ross, David P <ross.davidp@epa.gov>
Cc: Mclain, Jennifer <Mclain.Jennifer@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Mejias, Melissa <mejias.melissa@epa.gov>; Aguirre, Janita <Aguirre.Janita@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Wildeman, Anna <wildeman.anna@epa.gov>; Forsgren, Lee <Forsgren.Lee@epa.gov>; Wehling, Carrie <Wehling.Carrie@epa.gov>; Messier, Dawn <Messier.Dawn@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <hernandez.samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: For your review: Perchlorate - pass back language

Dave:
Attached for your review is the pass back document we prepared to respond to the OMB and the other federal agency comments received yesterday. The attached document (both in PDF and Word) reflect the changes we tentatively agreed to earlier today in our conversation with OMB staff.

Please advise if you are comfortable with our transmitting the attached document to OMB or if there are any further modifications you would like for us to make prior to sending. The perchlorate team and I will be ready to discuss any questions or comments you have at your earliest convenience.
Please note that we will be reviewing this mark-up concurrently with you to address any typographical errors that may have occurred while we were addressing OMB's comments.

Thanks for your continued support on this important action.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water

U.S. Environmental Protection Agency
202 564 5250

MEMORANDUM

SUBJECT: National Primary Drinking Water Regulations: Proposed Perchlorate Rule (Tier 1 Action; SAN 5555; RIN 2040-AF28) – **ACTION MEMORANDUM**

FROM: David P. Ross
Assistant Administrator (4101M)

THRU: Office of Policy (1803A)
Office of Executive Secretariat (1105A)

TO: Andrew J. Wheeler
Administrator (1101A)

PURPOSE

Attached for your signature is a proposed rule, titled "National Primary Drinking Water Regulations: Proposed Perchlorate Rule." We recommend signature and publication of this notice to solicit public comment on the EPA's proposal to establish a national primary drinking water regulation (NPDWR) and a non-enforceable maximum contaminant level goal (MCLG) for perchlorate under the Safe Drinking Water Act (SDWA). The proposed NPDWR includes an enforceable maximum contaminant level (MCL) of 0.056 mg/L (56 μg/L), which is proposed to be set at a level equal to the proposed MCLG. The EPA is seeking comment in the attached notice on whether the Agency should consider setting the perchlorate MCLG and MCL at alternative values of 0.018 mg/L (18 μg/L) and 0.090 mg/L (90 μg/L). The EPA is also seeking comment on whether it should withdraw the Agency's 2011 determination to regulate perchlorate in drinking water.

DEADINE/TIMELINE

In February 2011, the EPA published a final determination to regulate perchlorate in drinking water. Section 1412(b)(1)(A) of the SDWA requires that the EPA issue a proposed NPDWR within 24 months of the final regulatory determination and a final NPDWR within 18 months after the proposal. However, when the EPA consulted with the Science Advisory Board (SAB), the Agency received recommendations that the EPA prepare a pharmacokinetic model (i.e., a biologically based dose-response model [BBDR]) to predict the effects of perchlorate exposure on the thyroid function in pregnant women and their children, to develop the MCLG for perchlorate. The EPA collaborated with Food and Drug Administration scientists to perform the modeling recommended by the SAB and completed the analysis and associated peer reviews in March 2018.

In February 2016, the Natural Resources Defense Council (NRDC) filed a lawsuit for failure of the EPA to perform its mandatory duties of proposing and finalizing a regulation for perchlorate in accordance with timelines provided in the SDWA. The court-approved consent decree established deadlines for the EPA to sign a proposed rule by October 31, 2018, and a final rule by December 19, 2019.

The EPA was granted an extension on the consent decree for signature of the proposed rule until April 30, 2019. However, due to a partial government shutdown in early 2019, an additional extension was given for signature of the proposed rule until May 28, 2019. The EPA is addressing the consent decree requirements to sign a NPDWR and issue a MCLG for perchlorate in this proposed rule by May 28, 2019.

OVERVIEW

Perchlorate is an inorganic anion which occurs naturally. It is also manufactured as an oxidizer for rockets, missiles, and fireworks and can be an impurity in hypochlorite disinfectants. The public may be exposed to perchlorate through food and drinking water. When exposed, perchlorate interferes with the thyroid gland by inhibiting iodide uptake, which impacts the production of thyroid hormones that are crucial for normal growth and development. Poor iodide uptake in pregnant and lactating women is linked to delayed development and decreased learning capabilities in their infants.

The EPA proposes to establish a NPDWR and a MCLG and MCL of 0.056 micrograms per liter (mg/L) (56 ug/L) for perchlorate based on avoiding neurodevelopmental impacts in the most sensitive population, the children of pregnant women with low iodide intake. The standard is proposed at a level that will prevent these children from having intelligence quotient (IQ) decrements greater than 2 points and includes a margin of safety. The EPA proposes requirements for water systems to conduct monitoring and reporting on perchlorate, and to provide information on perchlorate levels to consumers. The EPA also proposes requirements for primacy agencies that implement the Public Water System Supervision program under the SDWA. The proposal includes a list of treatment technologies to enable water systems to comply with the MCL, including affordable technologies for small systems.

In the preamble to the proposed rule, the EPA presents the results of its economic analysis and the Agency's conclusion that the benefits of the proposed regulation do not justify the costs. The EPA seeks comment on whether the Agency should set the MCLG and MCL for perchlorate at alternative values of 0.018 mg/L (18 µg/L) and 0.090 mg/L (90 µg/L). These alternatives would avoid IQ decrements of 1 or 3 points, respectively, in the most sensitive population and include a margin of safety. Finally, the EPA seeks comment on whether it should withdraw the Agency's 2011 determination to regulate perchlorate in drinking water based on the new information that indicate perchlorate does not occur in public water systems with a frequency and at levels of public health concern. Under this alternative, the EPA would not issue a final MCLG or NPDWR for perchlorate.

The EPA has determined that the National Primary Drinking Water Regulations: Proposed Perchlorate Rule does not have disproportionately high and adverse human health or environmental effects on minority populations, low-income populations and/or indigenous

peoples, as specified in Executive Order 12898 (59 FR 7629, February 16, 1994), which establishes federal executive policy on environmental justice. This action would increase the level of environmental protection for all affected populations without having any disproportionately high and adverse human health or environmental effects on any population, including any minority or low-income population.

ANTICIPATED PUBLIC STAKEHOLDER RESPONSE

The EPA expects a variety of reactions and responses from stakeholders. Public health and environmental groups may state that proposed regulation is not sufficiently protective and that the EPA does not have the authority to withdraw a determination to regulate a contaminant under the SDWA. These groups may claim that the regulatory process, established in the 1996 SDWA amendments, is not functioning as intended because the EPA has not yet regulated a contaminant identified through the Contaminant Candidate List and Regulatory Determinations processes. Some stakeholders may be critical of the scientific analysis used to inform the derivation of the perchlorate MCLG and the estimate of benefits from the proposed regulation. Industry groups, including the American Water Works Association, the Perchlorate Study Group, the American Chemistry Council, and the U.S. Chamber of Commerce may state that the models have too much uncertainty and variability to be used to establish a drinking water standard.

INTERNAL DEVELOPMENT AND REVIEW PROCESS

The EPA workgroup consists of representatives from the Office of Water, the Office of Children's Health Protection, the Office of General Counsel, the Office of Policy, the Office of Research and Development, the Office of Land and Emergency Management, and the Office of Chemical Safety and Pollution Prevention. The Office of Water sought review and input of the draft *Federal Register* notice from this workgroup prior to submission for interagency review.

INTERAGENCY REVIEW

The Office of Management and Budget initiated review of the *Federal Register* notice: "National Primary Drinking Water Regulations: Proposed Perchlorate Rule" on April 15, 2019.

IMPACTS

The EPA estimates this proposed rule would impose an annual cost burden between $9.7 and $10.3 million. Approximately $3.1 to $3.2 million of that annual cost will be borne by states (and the Navajo Tribe) that have primacy to oversee implementation of the requirements. Between $6.6 and $7.1 million of the annual cost will be borne by public water systems and their rate payers. Monitoring and administration requirements are the majority of the annual cost. The EPA estimates that very few systems will have to install or operate treatment to comply with the regulation.

The EPA determined that the proposed regulation will result in annual costs that are less than one percent of revenue for small public water systems affected by this proposed rule. The average annual costs range from $88 to $94 for these systems. The EPA determined that the compliance costs for this action in any given year are less than the threshold set in the Unfunded Mandates Reform Act ($100 million in expenditures to state, local, and tribal governments in aggregate or to the private sector).

PEER REVIEW

The OW followed the EPA peer review policy with respect to the underlying scientific BBDR model used to derive an MCLG for perchlorate in this regulatory action. As stated above, the EPA sought recommendations from the SAB for developing the proposed MCLG.

To ensure that the EPA had implemented the SAB recommendations, the Agency convened an independent peer review panel to evaluate the BBDR models in 2017. The EPA considered all the recommendations from the 2017 peer review and implemented those needed to increase the scientific rigor of the model and modeling results.

The EPA convened a second, independent peer review panel in 2018 to evaluate the updates to the BBDR model. The EPA also presented several approaches to link the thyroid hormone changes in a pregnant mother predicted by the BBDR model to neurodevelopmental effects, using evidence from the epidemiological literature. The January 2018 peer review concluded that "the current models are fit for purpose to determine an MCLG."

RECOMMENDATION

I recommend that you sign the attached rulemaking, "National Primary Drinking Water regulations: Proposed Perchlorate Rule."

Attachment

MEMORANDUM

SUBJECT: National Primary Drinking Water Regulations: Proposed Perchlorate Rule

FROM: Eric G. Burneson, Director
Standards and Risk Management Division
Office of Ground Water and Drinking Water

TO: Anita M. Thompkins, Acting Director
Office of Ground Water and Drinking Water

Attached for your approval and transmittal to the Office of Water for review is a *Federal Register* notice titled: National Primary Drinking Water Regulations: Proposed Perchlorate Rule.

The EPA is proposing to establish a maximum contaminant level goal (MCLG) of 0.056 mg/L and a national primary drinking water regulation for perchlorate, which includes an enforceable maximum contaminant level (MCL) of 0.056 mg/L, as authorized under the Safe Drinking Water Act (SDWA). The action includes proposed requirements for public water systems to conduct monitoring and reporting on perchlorate and to provide information on perchlorate levels to consumers. The proposal includes a list of treatment technologies to enable water systems to comply with the MCL, including affordable technologies for small systems. The EPA is also proposing requirements for primacy agencies that implement the Public Water System Supervision program under the SDWA.

The *Federal Register* notice presents the EPA's economic analysis of the proposed perchlorate regulation and the Agency's conclusion that benefits of the proposed regulation do not justify the costs. The proposal includes the EPA's request for comment on alternative MCL/MCLG values of 0.018 mg/L and 0.090 mg/L. Finally, the EPA seeks comment on whether the Agency should withdraw the 2011 determination to regulate perchlorate in drinking water based on the new information that indicate perchlorate does not occur in public water systems with a frequency and at levels of public health concern. Under this alternative, the EPA would not issue a final MCLG or NPDWR for perchlorate.

I recommend that you approve and transmit the attached notice to the Office of Water for review. If you need additional information or have questions pertaining to any aspect of this notice, please call me or have your staff contact Samuel Hernandez at 202-564-1735.

Attachment

MEMORANDUM

SUBJECT: National Primary Drinking Water Regulations: Proposed Perchlorate Rule

FROM: Anita M. Thompkins, Acting Director
Office of Ground Water and Drinking Water

TO: David P. Ross
Assistant Administrator

Attached for your approval and transmittal to the Office of the Administrator is a *Federal Register* notice titled: National Primary Drinking Water Regulations: Proposed Perchlorate Rule.

The EPA is proposing to establish a maximum contaminant level goal (MCLG) of 0.056 mg/L and a national primary drinking water regulation for perchlorate, which includes an enforceable maximum contaminant level (MCL) of 0.056 mg/L, as authorized under the Safe Drinking Water Act (SDWA). The action includes proposed requirements for public water systems to conduct monitoring and reporting on perchlorate and to provide information on perchlorate levels to consumers. The proposal includes a list of treatment technologies to enable water systems to comply with the MCL, including affordable technologies for small systems. The EPA is also proposing requirements for primacy agencies that implement the Public Water System Supervision program under the SDWA.

The *Federal Register* notice presents the EPA's economic analysis of the proposed perchlorate regulation and the Agency's conclusion that benefits of the proposed regulation do not justify the costs. The proposal includes the EPA's request for comment on alternative MCL/MCLG values of 0.018 mg/L and 0.090 mg/L. Finally, the EPA seeks comment on whether the Agency should withdraw the 2011 determination to regulate perchlorate in drinking water based on the new information that indicate perchlorate does not occur in public water systems with a frequency and at levels of public health concern. Under this alternative, the EPA would not issue a final MCLG or NPDWR for perchlorate.

I recommend that you approve the proposed rule and sign the Action Memorandum, transmitting the attached notice to the Office of the Administrator for signature. If you need additional information or have questions pertaining to any aspect of this notice, please call me or have your staff contact Samuel Hernandez at 202-564-1735.

Attachment

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 4/5/2019 9:16:38 PM
To: Mclain, Jennifer [Mclain.Jennifer@epa.gov]; Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]
CC: Tiago, Joseph [Tiago.Joseph@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Flaharty, Stephanie [Flaharty.Stephanie@epa.gov]; Khera, Rajiv [Khera.Rajiv@epa.gov]; Flaharty, Stephanie [Flaharty.Stephanie@epa.gov]; Corr, Elizabeth [Corr.Elizabeth@epa.gov]
Subject: e-files for the perchlorate pkg
Attachments: Perchlorate Draft Action Memo 4-5-19.docx; Transmittal Memo AA to OPEI 4-5-19.docx; Transmittal Memo EB to JM 4-5-19.docx; Transmittal Memo JM to DR 4-5-19.docx

Jennifer: Attached please find updated transmittal memos to reflect the changes in the FRN notice for the perchlorate proposal. Please note that we have not attached the revised economic analysis. We informed OMB, OP and the OW-IO that we would require an additional week to revise this document.
Please let us know if you need any additional information.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: Hernandez-Quinones, Samuel
Sent: Friday, April 05, 2019 3:57 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Use this version - Comments: e-files for the perchlorate pkg

Revised Memorandums attached.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Burneson, Eric
Sent: Friday, April 05, 2019 1:47 PM
To: Khera, Rajiv <Khera.Rajiv@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Subject: FW: Use this version - Comments: e-files for the perchlorate pkg

Perchlorate team
Can we review and revise to be made to the other parts of this package to be consistent with the revised notice.
Thanks

From: Mclain, Jennifer
Sent: Friday, April 05, 2019 12:28 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: FW: Use this version - Comments: e-files for the perchlorate pkg

Eric – is your team working on any updates to the package that may be needed to incorporate the changes we made to the draft proposed rule?

From: Tiago, Joseph
Sent: Wednesday, March 06, 2019 1:32 PM
To: Evalenko, Sandy <Evalenko.Sandy@epa.gov>; Lousberg, Macara <Lousberg.Macara@epa.gov>
Cc: Burneson, Eric <Burneson.Eric@epa.gov>; Mclain, Jennifer <Mclain.Jennifer@epa.gov>; Fields, Wanda <Fields.Wanda@epa.gov>
Subject: RE: Use this version - Comments: e-files for the perchlorate pkg

Hi Sandy,

Thank you for your edits. Your changes have been accepted and two typos corrected as follows:

DR to AW Memo:
Under Impacts: …and administration requirements consisted of the majority of the annual cost.

DR to BB Memo:
This action presents the results of the EPA's economic analysis of the proposed perchlorate regulation and the Agency's conclusion that benefits of the proposed regulation do not justify the costs.

Let me know if you have any questions.

Joe.

From: Evalenko, Sandy
Sent: Wednesday, March 6, 2019 1:08 PM
To: Tiago, Joseph <Tiago.Joseph@epa.gov>; Lousberg, Macara <Lousberg.Macara@epa.gov>
Cc: Burneson, Eric <Burneson.Eric@epa.gov>; Mclain, Jennifer <Mclain.Jennifer@epa.gov>; Fields, Wanda <Fields.Wanda@epa.gov>
Subject: RE: Use this version - Comments: e-files for the perchlorate pkg

I think you mean the NPRM – the rule is attached.
If not, let me know.
Sandy

From: Tiago, Joseph
Sent: Wednesday, March 06, 2019 1:05 PM
To: Evalenko, Sandy <Evalenko.Sandy@epa.gov>; Lousberg, Macara <Lousberg.Macara@epa.gov>
Cc: Burneson, Eric <Burneson.Eric@epa.gov>; Mclain, Jennifer <Mclain.Jennifer@epa.gov>; Fields, Wanda <Fields.Wanda@epa.gov>
Subject: RE: Use this version - Comments: e-files for the perchlorate pkg

Thanks, Sandy!

Note the EO 12866 file is blank – not sure it was intentional.

We'll get you a revised version of the memos.

Joe.

From: Evalenko, Sandy
Sent: Wednesday, March 6, 2019 12:59 PM
To: Tiago, Joseph <Tiago.Joseph@epa.gov>; Lousberg, Macara <Lousberg.Macara@epa.gov>
Cc: Burneson, Eric <Burneson.Eric@epa.gov>; Mclain, Jennifer <Mclain.Jennifer@epa.gov>; Evalenko, Sandy <Evalenko.Sandy@epa.gov>; Fields, Wanda <Fields.Wanda@epa.gov>
Subject: Use this version - Comments: e-files for the perchlorate pkg
Importance: High

In this version, I also added the San and Rin in the subject line for the Transmittal memo.

Thanks for sending the Perchlorate package. I have a few edits/comments.

1. Thank you for preparing both a transmittal memo and draft action memo. Attached are comments and suggestions.

2. A minor edit regarding the NPRM file name and OMB's requirements. OMB is particular regarding the naming convention. I added the title to the first page of the FRN and changed the title of the Proposed Rule file to

   EO12866_SDWA NPDWR Perchlorate 2040-AF28 NPRM 20190305

3. I removed the first paragraph of the Tribal EO (see below) – which was the 1st paragraph in the old template. I did not change anything else in the body/text of the Tribal EO.

Executive Order 13175, entitled ''Consultation and Coordination with Indian Tribal Governments'' (65 FR 67249, November 9, 2000), requires the EPA to develop "an accountable process to ensure meaningful and timely input by Tribal officials in the development of regulatory policies that have Tribal implications." The definition of ''policies that have Tribal implications'' includes regulations that have "substantial direct effects on one or more Indian Tribes, on the relationship between the federal government and the Indian Tribes, or on the distribution of power and responsibilities between the federal government and Indian Tribes." Under Executive Order 13175, the EPA may not issue a regulation that has Tribal implications, that imposes substantial direct compliance costs, and that is not required by statute, unless the federal government provides the funds necessary to pay the direct compliance costs incurred by Tribal governments, or the EPA consults with Tribal officials early in the process of developing the proposed regulation and develops a Tribal summary impact statement.

Please send me the final versions of the memos and I'll print them.

Sandy

From: Lousberg, Macara
Sent: Tuesday, March 05, 2019 7:22 PM
To: Tiago, Joseph <Tiago.Joseph@epa.gov>
Cc: Evalenko, Sandy <Evalenko.Sandy@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Mclain, Jennifer

<Mclain.Jennifer@epa.gov>
Subject: Fwd: e-files for the perchlorate pkg

Thanks Joe. Looping in Sandy.

Did you all get any comments from Anna or Lee?

Sent from my iPhone

Begin forwarded message:

> **From:** "Tiago, Joseph" <Tiago.Joseph@epa.gov>
> **Date:** March 5, 2019 at 5:27:53 PM EST
> **To:** "Lousberg, Macara" <Lousberg.Macara@epa.gov>
> **Cc:** "Burneson, Eric" <Burneson.Eric@epa.gov>, "Mclain, Jennifer" <Mclain.Jennifer@epa.gov>
> **Subject: FW: e-files for the perchlorate pkg**
>
> Hi Macara,
>
> Please find attached the Perchlorate FRN package for review and processing. I'm bringing the hard copy of the package to you shortly.
>
> Let me know if you have any questions.
>
> Regards,
>
> Joe.

Message

From: Strong, Jamie [Strong.Jamie@epa.gov]
Sent: 3/25/2019 3:04:50 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: perchlorate paper on model
Attachments: clewell et al 2019.pdf

Lisa,
I am sure you have already seen this, but I wanted to pass this along to you in case you hadn't. They offer some hefty criticisms of the model, have you reached out to Paul S about this publication? I expect you may hear some of the same from some interagency reviewers or public.

Jamie

https://insideepa.com/daily-news/scientists-back-use-2007-risk-approach-epa-perchlorate-standard

Scientists Back Use Of 2007 Risk Approach For EPA Perchlorate Standard

March 15, 2019
A team of scientists in an article accepted for publication in the journal *Regulatory Toxicology and Pharmacology* is backing the American Water Works Association's (AWWA) call for EPA to rely on a 2005 risk assessment in crafting a perchlorate drinking water standard that could spur a weaker limit than use of an alternative approach.
The recommendation from the team of five is at odds with findings from a peer review panel that in 2018 advocated for a modeling method that could justify a more-stringent perchlorate limit.
The article by the team of five says that while EPA's 2017 biologically-based dose-response (BBDR) model "represents a valuable research tool, the lack of supporting data for many of the model assumptions and parameters calls into question the fitness of the extended BBDR model to support quantitative analyses for regulatory decisions on perchlorate in drinking water."
It was written by Harvey H. Clewell, III, a principal consultant with the company Ramboll, and others including fellow consultants and Eric Hack, a research scientist with the company ScitoVation.
The team says that until more data can be developed to address uncertainties in the current BBDR model, EPA should continue to rely on the 0.7 microgram per kilogram bodyweight per day reference dose (RfD) the National Academy of Sciences recommended in 2007, the article says.
AWWA, which represents drinking water utilities, funded the analysis but was not involved in writing the article. The group has previously argued in favor of using the RfD in developing a future EPA perchlorate standard rather than alternative approaches.
EPA is under a judicial deadline of April 30 to propose a health-based maximum contaminant level goal (MCLG) and related enforceable drinking water standard for the rocket fuel ingredient perchlorate that takes into account technical feasibility and cost.
The article's findings differ from a contractor-run peer review panel that last year concluded in its final report, "Overall, the panel agreed that the EPA and its collaborators have prepared a highly innovative state-of-the-science set of quantitative tools to evaluate neurodevelopmental effects that could arise from drinking water exposure to perchlorate. While there is always room for improvement of the models, with limited additional work to address the committee's comments below, the current models are fit-for-purpose to determine an MCLG."
At a public meeting prior to the peer reviewers' report, one of the reviewers, Hugh Barton, reacted with surprise when AWWA Manager of Federal Relations Kevin Morley in public comments suggested that "the best available science goes back to the RfD . . . as most suitable for regulatory development."
After questioning Morley about the traditional calculation for a drinking water standard from an RfD, based on adult consumption and weight estimates, Barton said, "I'd be concerned that at a public drinking water [level of 24.5 parts per billion] that perchlorate would become the next Flint, Michigan."
Barton expanded on his concerns of using the RfD to form the basis for the MCLG at the end of the meeting, noting that EPA's proposed analysis in 2012 discussed various consumption rates and body weights for infants, children and/or pregnant women to set a standard protective of the most sensitive subpopulation -- the fetuses of women with hypothyroxinemia, or low iodine levels. Iodine is necessary for crucial neurodevelopment, and the fetus is dependent upon the mother for iodine.
Barton noted that EPA's 2012 analysis resulted in as much as a 10-fold difference in potential drinking water standards "because of the volume [of water consumed] per bodyweight." Of most concern to him, the analysis resulted in the same potential standard for pregnant and non-pregnant women, despite the difference in their iodine needs. "The simple calculation from the RfD that says they're the same is not particularly credible."
Authors' Findings

But Clewell and his co-authors say that while the hormone component of the BBDR model is "a scientific improvement in terms of incorporating the available biology, there is a lack of data to provide critical validation in multiple steps of the proposed approach and to support several assumptions/parameters within the BBDR model."

While no major structural defects in EPA's model were identified, there are uncertainties in the model parameterization that call into question its use for predicting very small changes in clinical hormone values, such as a 1 percent change in free tetraiodothyronine (fT4) that may result in an increase in the prevalence of hypothyroxinemia in pregnant women, the article says. Hypothyroxinemia is often associated with hypothyroidism, or low concentrations of fT4, despite increased concentrations of thyroid stimulating hormone.

While the model prediction for a 1 percent change in fT4 would yield a point of departure, or starting point for later analysis of the dose-response curve, lower than EPA's RfD, "that level of precision is a not supported by the comparison of the model predictions with available data," the article says. Comparing the point of departure from EPA's 2005 Integrated Risk Information System assessment of perchlorate with the points of departure calculated by the BBDR model shows the RfD "is protective for all of the endpoints from epidemiological studies and is consistent with a change in population fT4 levels of less than 5%."

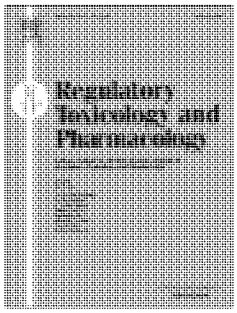
The fundamental underpinning of the agency's risk assessment approach has been the use of an obligatory precursor as a conservative basis for protecting against downstream health effects, the article says.

But "[u]nless perchlorate concentrations in the blood are sufficient to disrupt iodine uptake, there is no plausible basis for suggesting an effect of perchlorate on thyroid hormone homeostasis or subsequent events leading to developmental or (in the rat) carcinogenic effects. The recent studies suggesting a relationship between perchlorate exposure and decreased fT4 do not impeach this causal relationship."

Therefore, until the significant uncertainties in the current BBDR model and draft MCLG approaches can be addressed, EPA should continue to rely on the RfD approach based on inhibition of thyroidal iodine uptake for any further regulatory action, the article says.

The EPA "RfD includes an intraspecies uncertainty factor of 10 'to protect the most sensitive population, the fetuses of pregnant women who might have hypothyroidism or iodide deficiency.' None of the predictions of the BBDR model suggest that this uncertainty factor is inadequate," the article says. -- *Lara Beaven* (lbeaven@iwpnews.com)

Accepted Manuscript



An evaluation of the USEPA Proposed Approaches for applying a biologically based dose-response model in a risk assessment for perchlorate in drinking water

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An Evaluation of the USEPA Proposed Approaches for Applying a Biologically Based Dose-Response Model in a Risk Assessment for Perchlorate in Drinking Water

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ABSTRACT

The United States Environmental Protection Agency's (USEPA) 2017 report, "Draft Report: Proposed Approaches to Inform the Derivation of a Maximum Contaminant Level Goal for Perchlorate in Drinking Water", proposes novel approaches for deriving a Maximum Contaminant Level Goal (MCLG) for perchlorate using a biologically-based dose-response (BBDR) model. The USEPA (2017) BBDR model extends previously peer-reviewed perchlorate models to describe the relationship between perchlorate exposure and thyroid hormone levels during early pregnancy. Our evaluation focuses on two key elements of the USEPA (2017) report: the plausibility of BBDR model revisions to describe control of thyroid hormone production in early pregnancy and the basis for linking BBDR model results to neurodevelopmental outcomes.. While the USEPA (2017) BBDR model represents a valuable research tool, the lack of supporting data for many of the model assumptions and parameters calls into question the fitness of the extended BBDR model to support quantitative analyses for regulatory decisions on perchlorate in drinking water. Until more data can be developed to address uncertainties in the current BBDR model, USEPA should continue to rely on the RfD recommended by the NAS (USEPA 2005) when considering further regulatory action.

Keywords: perchlorate, risk assessment, MCLG, BBDR model

INTRODUCTION

From a regulatory perspective, the critical effect of concern from exposure to perchlorate is disruption of thyroid function and the potential for thyroid-hormone-related effects on neurodevelopment in gestation; these effects represent downstream events resulting from competitive inhibition of iodide uptake by the perchlorate ion (USEPA 2002). Based on an analysis of the mode of action for perchlorate, the United States Environmental Protection Agency (USEPA) (2002) determined that inhibition of thyroid iodide uptake could be used as an obligatory precursor for these critical effects in a harmonized cancer/noncancer risk assessment for perchlorate (Figure 1). This mode-of-action directed risk assessment approach was used in the derivation of the current Reference Dose (RfD) for perchlorate of 0.0007 mg/kg/day (USEPA 2005). Following the recommendations of the National Academy of Sciences National Research Council (NRC) (2005), the point of departure (POD) for this RfD was a reported No Observed Effect Level (NOEL): a non-statistically significant mean of 1.8% (standard error of the mean 8.3%) decline in radioactive iodine uptake (RAIU) in healthy adults following two weeks exposure to a daily perchlorate dose of 0.007 mg/kg/day (Greer et al. 2002). An intraspecies uncertainty factor of 10 was applied to protect the most sensitive population, the fetuses of pregnant women who might have hypothyroidism or iodide deficiency.

Subsequently, the USEPA Office of Drinking Water (2008) published an Interim Health Advisory Level for perchlorate of 15 µg/L, based on the USEPA (2005) RfD of 0.7 µg/kg/day, as recommended by the NRC (2005). Determination of this Interim Health Advisory Level considered Physiologically-Based Pharmacokinetic (PBPK) Modeling (Clewell et al. 2007) to estimate the potential effect of perchlorate on iodide uptake in several sensitive subgroups, including the pregnant woman and fetus, the lactating woman and neonate, and the young child. Despite widespread scientific acceptance of iodide inhibition as an obligatory precursor to downstream toxicity endpoints, there was remaining concern regarding the level of protection for the population perceived to have the greatest susceptibility – the fetuses of hypothyroid mothers.

Over the next several years, the focus of research on perchlorate shifted to the development of a biologically based dose-response (BBDR) model of the hypothalamic-pituitary-thyroid (HPT) axis that could be linked with the PBPK model of perchlorate and iodide to predict dose-dependent interactions

of perchlorate with iodine hormone homeostasis as a function of iodide intake in an effort to more quantitatively account for the effects of low dietary iodide intake and hypothyroidism in pregnant women on fetal development (McLanahan et al. 2008, 2009; Fisher et al. 2012; Lumen and George 2017a, 2017b; Lumen et al. 2013, 2015).

The USEPA Science Advisory Board (SAB) (2013) report on perchlorate in drinking water supported the utility of BBDR modeling to help characterize the potential for neurological effects from perchlorate exposure:

> "As perchlorate research continues, studies in animals may provide important insights into the neurobehavioral consequences of perchlorate exposure. A physiologically-based pharmacokinetic/pharmacodynamic framework is well suited to help place these findings in the context of human perchlorate exposure."

The USEPA SAB (2013) identified a number of areas for improvement or modification of the existing models. However, they also noted that "Models can always be improved, but the goal is to have a model that is fit for the intended purpose.", apparently cautioning against perpetual model refinement at the expense of implementation, echoing the concern of the renowned statistician, George E.P. Box, who famously used to say: "All models are wrong but some are useful" (Box 1976).

Recently, the USEPA's Office of Ground Water and Drinking Water (USEPA 2017) responded to the Science Advisory Board recommendations and proposed novel approaches to inform the derivation of a Maximum Contaminant Level Goal (MCLG) for perchlorate, including the use of BBDR modeling in their report entitled "Draft Report: Proposed Approaches to Inform the Derivation of a Maximum Contaminant Level Goal for Perchlorate in Drinking Water". This MCLG approach (USEPA 2017) includes revisions to a previously developed and peer reviewed BBDR model (McLanahan et al. 2008, 2009; Fisher et al. 2012; Lumen and George 2017a, 2017b; Lumen et al. 2013, 2015) that was extended to predict the relationship between perchlorate exposure and thyroid hormone levels in sensitive life stages. These revisions aim to address suggestions by the USEPA SAB (2013), including the following:

- Derivation of a perchlorate MCLG that addresses sensitive life stages through PBPK/PD modeling;

- Expansion of the modeling approach to account for thyroid hormone perturbations and potential adverse neurodevelopmental outcomes from perchlorate exposure;
- Utilization of a mode of action framework for developing the MCLG that links the steps in the proposed mechanism leading from perchlorate exposure through iodide uptake inhibition to thyroid hormone changes and finally neurodevelopmental impacts; and
- Extension of "the [BBDR] model expeditiously to…provide a key tool for linking early events with subsequent events as reported in the scientific and clinical literature on iodide deficiency, changes in thyroid hormone levels, and their relationship to neurodevelopmental outcomes during sensitive early life stages" (USEPA SAB 2013, p. 19).

Model revisions presented in the USEPA (2017) report include: incorporating a description of the physiology of early pregnancy, biological feedback control of hormone production via thyroid-stimulating hormone (TSH) and human chorionic gonadotropin (hCG), and a description of the response to lower levels of iodide nutrition. In addition, an attempt was made to calibrate the model's behavior for upper and lower percentiles of the population, in addition to the population median, for thyroid hormone production. The report also included an uncertainty analysis for key BBDR model parameters.

For the development of the MCLG, USEPA (2017) proposed a two-stage approach linking the revised BBDR model results ("Stage 1") with quantitative information on neurodevelopmental outcomes from epidemiological studies ("Stage 2"). Stage 1 describes the thyroidal hormone levels in women of childbearing age with low to adequate iodide intake. In this stage, the revised BBDR model is applied to predict the relationship between perchlorate exposure and changes in thyroid hormone levels in early pregnancy. Data for Stage 2 of the approach is provided from epidemiological studies evaluating maternal thyroid hormone levels in early pregnancy and the relationship between changes in these levels and the observation of neurodevelopmental outcomes. The USEPA (2017) report also described development of a novel population-based approach that uses the revised BBDR model to estimate changes in levels of selected thyroid hormones, specifically free tetraiodothyronine (fT4) and TSH, resulting from perchlorate exposure that may result in an increase in the prevalence of hypothyroxinemia in pregnant women. Hypothyroxinemia (low circulating concentrations of fT4) is

111 often associated with hypothyroidism (low concentrations of fT4 despite increased concentrations of
112 TSH).

113 The evaluation and (potential) application of the perchlorate BBDR model will serve as an important
114 precedent for future consideration of such models by the agency, as it is only the second such model
115 to be seriously evaluated by USEPA and subjected to external peer-review. The first BBDR model to
116 be considered, formaldehyde nasal carcinogenicity developed by Conolly and colleagues (2003, 2004),
117 has been under consideration by the agency for more than a decade. Interest in the use of BBDR
118 modeling in risk assessment peaked in the 1990s when the draft USEPA (2003) Cancer Guidelines
119 identified these models as the preferred option for performing a cancer dose-response. However,
120 since that time, work in this area has waned, possibly due to the perceived difficulty of gaining
121 regulatory acceptance. By their nature, BBDR models are descriptions of complex biological systems
122 that necessarily include significant uncertainty. The challenge going forward will be to develop
123 approaches for characterizing that uncertainty in a risk assessment context and ensuring that these
124 complex models are fit for their intended purpose. It is with this consideration in mind that we have
125 performed a focused evaluation of the proposed USEPA (2017) approaches.

126 Our critical review focused on two key areas of importance for determining whether the current BBDR
127 model is fit for the purpose of supporting regulatory decisions based on predicted effect of perchlorate
128 exposure on human fetal development:

129 1. Evaluation of USEPA (2017) model revisions to the peer reviewed BBDR models, including
130 extending the model to early pregnancy, incorporating biological feedback control of hormone
131 production via thyroid stimulating hormone (TSH) and human chorionic gonadotropin (hCG)
132 signaling, calibration of the model for thyroid hormone effects, and uncertainty analysis for
133 key parameters. This evaluation included comparison of model output to results from key
134 human studies identified in previous assessments (Greer et al. 2002, Braverman et al. 2006,
135 Téllez et al. (2005a, 2005b), as well as in the USEPA (2017) document (Steinmaus et al.
136 2016);
137 2. Evaluation of USEPA (2017) approaches for linking BBDR results to neurodevelopmental
138 outcomes and identification of published literature to develop the quantitative relationship
139 between thyroid hormone levels and neurodevelopmental outcomes; and

After describing the results of this evaluation, we present a comparison of the results from the USEPA (2017) approach with results from previous USEPA assessments, in order to put the uncertainties in the BBDR approach in perspective against the potential impact of the new approach on the existing regulatory guidelines for perchlorate USEPA (2005, 2008).

METHODS

Evaluating Stage 1 of USEPA MCLG approach: Stage 1 of USEPA's MCLG approach relies upon the application of the BBDR model to predict the effect of perchlorate on the thyroid hormone in pregnant women at different iodine nutrition levels, with the goal of predicting fT4 hormone reduction in pregnant women with low dietary iodide. To evaluate the utility of the proposed model to support such predictions, we independently ran the model and tested model predictions against data from multiple studies. These exercises attempted to both duplicate BBDR model results for datasets that were used by USEPA (2017) to calibrate the model and to test the ability of the BBDR model to predict the well-described precursor event inhibition of iodide uptake, which was successfully described with previous versions of the perchlorate PBPK models (Merrill et al. 2003; Clewell et al. 2007). These simulations included:

- Steinmaus et al. 2016 – cross-sectional epidemiological study evaluation of serum and urine in pregnant women in California: used in USEPA (2017) to evaluate BBDR model predictions of perchlorate effects on fT4 and TSH
- Greer et al. 2002 – 14-day controlled perchlorate dose study in male and female adults in the US: used in USEPA (2017) to estimate urinary clearance parameters in BBDR model
- Braverman et al. 2006 – 6-month controlled perchlorate dose study in male and female adults: not used in USEPA (2017)
- Téllez Téllez et al. 2005a, 2005b – longitudinal epidemiological study in pregnant and lactating women in Chile: used in USEPA (2017) to estimate urinary clearance parameters in BBDR model

In our efforts to produce these simulations, it was noted that instructions provided in the USEPA documentation for running the model for different scenarios, and documentation of the rationale for the model parameter values associated with them, are often inadequate and lack transparency; this deficiency is exacerbated by the number of permutations of parameter settings used in the scripts that

generate the results in the document. The complexity of the BBDR model makes it difficult to perform this evaluation, even though it has been conducted by experienced modelers.

Evaluating Stage 2 of USEPA MCLG approach: Stage 2 of USEPA's approach involved evaluating the published epidemiological literature to identify publications that would define quantitative relationships between thyroid hormone levels and neurodevelopmental effects. The USEPA approach was focused on the identification of studies that provided information on levels of fT4 in pregnant mothers during early gestation and the potential for changes in neurodevelopmental outcomes in their offspring. Through targeted literature searching and recommendations from the Science Advisory Board (SAB), a total of 55 studies were identified by USEPA to provide information on altered maternal thyroid hormone levels and offspring development. These studies were divided into three groups to facilitate evaluation:

- Group 1 – studies that may be able to quantitatively describe a relationship between incremental alterations in maternal thyroid hormone levels and alternations in offspring development;
- Group 2 – studies that do not have data from which to derive a quantitative relationship between maternal hormones and offspring neurodevelopment, but instead present only a categorical analysis with thyroid hormones below and above a defined cut point and adverse neurodevelopmental outcomes; and
- Group 3 – studies that present an analysis that is not directly compatible with BBDR output.

Of the 55 studies, 15 were identified as Group 1, 14 were identified as Group 2, 26 were identified as Group 3. The 15 Group 1 studies were then evaluated further and only 5 were deemed useful by the USEPA for further quantitative analysis to attempt to connect alterations in thyroid hormone levels to alterations in neurodevelopment. in our evaluation, we performed a critical review of the USEPA Stage 2 approach and the study summaries provided in USEPA (2017), considering the most recent recommendations from the National Research Council (NRC 2014) on systematic review of the literature and evidence integration.

RESULTS

Evaluation of the Perchlorate BBDR Model for Early Pregnancy

The draft MCLG approach (USEPA 2017) is based on a hypothesized mode of action (Figure 1) for neurodevelopmental outcomes resulting from development of hypothyroxinemia from perchlorate-induced inhibition of iodide uptake in the thyroid. As noted in USEPA (2017):

> "Thyroid hormones are essential for the development and differentiation of the developing brain. The brain and spinal cord begin development in the first half of the first trimester. fT4 passes through the blood-brain barrier via multiple, specific transporter proteins. Next, T4 is converted to T3 by the developing glial cells and then transported to neurons. T3 then interacts with nuclear receptors to tightly regulate gene expression so that neurogenesis, synaptogenesis, neuronal migration, cell differentiation, and myelination are developmentally appropriate. Deficiencies in thyroid hormones through iodine deficiency, congenital hypothyroidism, or maternal hypothyroidism/hypothyroxinemia can result in neurological impairments and intellectual deficits (Morreale de Escobar, Obregón, & Escobar del Ray 2000)."

As recommended by the USEPA SAB (2013), the USEPA extended a published BBDR model for perchlorate induced hypothyroxinemia in late gestation (Lumen et al. 2013; Lumen and George 2017a, 2017b) to address the sensitive population of concern for exposure to perchlorate: the fetuses of hypothyroxinemic women during early pregnancy (Figure 2). These concerns were motivated by new studies (Steinmaus et al. 2016), suggesting an association between perchlorate exposure and decreased levels of free thyroxine (fT4) in pregnant women. Because the fetus is entirely dependent on maternal thyroid hormones for neurodevelopment in early gestation (Clewell et al. 2007; Howdeshell 2002), the endpoint of interest was defined as reduction in maternal fT4 in early pregnancy and the perchlorate BBDR models were extended to describe hormone homeostasis during gestation. Expansion of the original models of perchlorate and iodide (Clewell et al. 2007) to predict the impact of perchlorate exposure on fT4 during early pregnancy, however, is complicated by the significant variability in the levels of fT4 in the general population and the challenges in measuring fT4, as well as the dynamics of changing hormones through the course of gestation and the uncertainty in identifying the level of alteration that may lead to hypothyroidism and fetal effects.

224

225 According to the "American Thyroid Association Task force on Thyroid Disease During Pregnancy and
226 Postpartum", isolated hypothyroxinemia is defined as a normal maternal TSH concentration in
227 conjunction with fT4 concentrations in the lower 5th or 10th percentile of the reference range
228 (Stagnaro-Green et al. 2011). USEPA (2017) has also focused on selected percentiles of the reference
229 range; however, reference ranges can vary from population to population according to the *2017*
230 *Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease*
231 *During Pregnancy and Postpartum* (Alexander et al. 2017). Even within US populations and across
232 ethnic groups, the 2.5th percentile can vary by up to 2 pmol/L or approximately 20% (9.3-11.4
233 pmol/L as reported by Alexander et al. 2017).

234 The variation in fT4 reported in the published literature during early pregnancy is provided in USEPA
235 (2017), Appendix A, Figure A-33 and reproduced in Figure 3. The levels of fT4 during early
236 pregnancy, based on the studies identified by USEPA (2017), appear to range from approximately 13-
237 17 pmol/L. This range is consistent with the range of baseline fT4 means reported in the Greer et al.
238 (2002) study of approximately 1.1 – 1.3 ng/dL (14 - 17 pmol/L). However, the 50th percentile BBDR
239 model predictions at zero dose perchlorate and 170 µg/day iodine intake are approximately 10 pmol/L
240 at gestation weeks 12, 13, and 16, considerably below these reported values.

241

242 Measuring fT4 in the presence of high concentrations of bound T4 is challenging, especially in
243 conditions where binding proteins are altered such as during pregnancy (Alexander et al. 2017).
244 Measurement techniques are prone to inaccuracy during pregnancy due to disruption of the original
245 equilibrium. The 95% fT4 reference intervals decrease gradually with advancing gestational age: from
246 1.08– 1.82 ng/dL (approximately 13.9 – 23.5 pmol/L) in week 14 to 0.86–1.53 ng/dL (approximately
247 11.1 – 19.8 pmol/L) in week 20 (Alexander et al. 2017).

248 Extending the thyroid BBDR model to address early gestation is particularly challenging due to
249 the complex interaction between thyroid homeostasis and gestational development.
250 Considering the addition of TSH feedback dynamics, and an adjustment factor to match
251 specific population percentiles, there is reason for concern regarding the uncertainty of the

revised model predictions under low iodide intake conditions. Some of these concerns are highlighted below:

Description of hCG dynamics: Human chorionic gonadotropin (hCG) levels rise in early pregnancy and this in turn increases both sodium-iodide symporter (NIS) uptake activity and T4 production. hCG is structurally similar to TSH and, like TSH, increases thyroidal iodide uptake and thyroid hormone synthesis by binding to the thyroid-stimulating hormone receptor (TSHR) (Hoermann et al. 1994). In the model, hCG levels are calculated as a function of gestational age, using an equation for the parameter HCGREG (Figure 4, purple curve), and these changing levels are used to increase the rate of T3 and T4 production as a function of the hCG concentration:

$$HCGreg = 1 + 0.00354*hCG$$

The variation of hCG over the duration of gestation is based on direct measurements of hCG in pregnant women (Korevaar et al. 2015). However, the concurrent increase in thyroidal iodine uptake is described in the model based on an empirical relationship between gestational age in weeks (GW) and radioactive iodide uptake, using an equation for the parameter VCHNG (Figure 4, green curve):

$$VCHNG(GW) = 1 + 0.076 \cdot GW - 0.0025 \cdot GW^2$$

Thus the model does not correctly attribute the gestational control of NIS uptake to hCG, when in fact both uptake and hormone synthesis respond to the same changes in hCG (Pesce and Kopp 2014). By using different equations for the time-dependence of hCG-stimulated uptake and hormone production (Figure 4) the model decouples processes that are fundamentally linked by their biology. Figure 4 depicts the time-course of the parameters controlling changes in iodide uptake (VCHNG) and hCG hormone levels (HCGreg) over the course of gestation. While the biology indicates a proportional relationship between the two parameters, the equations used in the model are not parallel. Elucidating the impact of this decoupling is challenging, and is beyond the scope of this review, since it would have to be investigated at a large number of time-points throughout pregnancy and under different conditions of iodine intake, but the disparity between the model description and the underlying biology justifies caution regarding its predictions of T4 and TSH at different gestational ages, as these parameters govern hormone production and

release. We address the impact of the discrepancy between the time-courses for HCGREG and VCHNG in a later section.

Damping of TSH response: The USEPA (2017) BBDR model includes a parameter, pTSH (power to which the ratio of current TSH to the TSH set-point is raised), that reduces the response of the thyroid to increases in TSH:

$$TSHreg = (TSH/TSH_0)^{pTSH}$$

Using this equation, a pTSH exponent of 0 would represent no control of thyroid function by TSH and an exponent of 1 would represent a linear response of thyroid function to changes in TSH. In their calculations of the effect of perchlorate on the prevalence of hypothyroxinemic pregnant women, the USEPA (2017) use a pTSH exponent of 0.398, which results in a response to TSH that is substantially less than linear, an assumption that is inconsistent with the fundamental biological relationship between TSH and thyroid hormones (production and release of T3 and T4), effectively decoupling a relationship that has been well established in the medical, pharmacological and toxicological communities. USEPA (2017) describes the rationale for this parameter: "The NHANES data do not show a clear correlation between TSH and fT4, so within that data set they vary independently. One could assume, therefore, that individuals with an average fT4 and high TSH have that combination because their thyroid has a weak response to TSH, and vice-versa." To address this concern, USEPA (2017) estimated a lower and upper bound for pTSH as (median TSH)/(97.5th percentile TSH) = 0.398 and (median TSH)/(2.5th percentile TSH) = 3.09, respectively, with a median value of pTSH = 1. Thus, this parameter is used to attempt to represent disease states where the individual's thyroid is either exquisitely sensitive or insensitive to TSH stimulation. At lower values, this parameter reduces the impact of TSH on the Vmax for thyroid iodide uptake as well as the rate constants for T4 and T3 production in the thyroid. However, the USEPA (2017) also states that: "The coefficient, pTSH, is included…to allow for tuning of the strength of the TSH feedback, but in practice model simulations versus data appear quite adequate with pTSH=1." Concerns about this parameter are two-fold. First, the complexity of the model and various runtime scripts makes it nearly impossible to determine the use of this

parameter during some of the model assessment and risk assessment simulations presented in USEPA (2017). Second, using point estimate population level data to define the quantitative temporal relationship between two fundamentally linked processes at the individual level is scientifically inappropriate. To understand the biological feedback within a single individual (i.e. to determine the relationship of TSH to T3/T4 and Vmax for a hypothyroid or hyperthyroid individual), matched samples would be needed for TSH, T3 and T4. This information – to our knowledge – is not available from NHANES. Thus, the epidemiological point estimate data are being used well beyond its domain of applicability to predict the quantitative outcome of disease states.

Calibration of hormone production rates: The model uses a baseline first-order constant calibrated to NHANES 2007-2012 median, 10th, or 90th percentile non-pregnant data (fT4, fT3, T4 and T3 concentrations). The model parameter for the rate of production of T4 (KProdT4F) for the median NHANES calibration used in USEPA (2017) is 6.25*10-7 /hr/$kg^{0.75}$ (their Table A-2), which is 4-fold lower than the value of 2.45 x 10-6 estimated for the published model (Lumen et al. 2013), which was based on the data of Nicoloff et al. (1972). However, the use of a T4 production rate that is lower than the published value is not adequately justified, given the importance of this parameter, which has a direct impact on predictions of fT4 changes, the intended application of the model. This baseline value is then scaled in pregnancy through GW 16 (peak occurring ~ GW 9) based upon placental hCG increase over this time, according to the linear relationship from Glinoer (1997): hCGreg = 1 + 0.00354 x hCG.

Affinity of NIS Iodine uptake: The model uses a Km for perchlorate binding to the NIS (KmNIS_P) that is 3-fold lower than the value estimated by Lumen et al. (2013) (i.e. a 3-fold higher affinity). Specifically, the new Km represents the 2.5th percentile lower confidence limit of the population median based upon the USEPA (2017) reanalysis of Greer et al. (2002). The median value (50th percentile = 0.73 µM) is similar to that obtained from a re-analysis of *in vitro* binding data, 0.59 µM (Schlosser 2016); the use of a value of KmNIS_P = 0.489 µM makes perchlorate 3 times more effective at competitive inhibition of NIS compared to the model of Lumen et al. (2013). This revision to the Km in USEPA (2017) necessitated revisions to the Vmax (VmaxNISF_thy_P) and urinary excretion parameters (CLFUP) (Table 1 of USEPA 2017), further affecting the model's

sensitivity to changes in perchlorate dose, particularly under conditions of low iodide. Thus, The USEPA (2017) BBDR model predicts much greater effects of perchlorate on iodide uptake than any previous version of the model, without justification for re-estimating these parameters rather than using the published values.

Assumptions regarding thyroidal iodide storage: Plots of NHANES 2007-2012 data for non-pregnant women demonstrated little relationship between iodine intake and fT4, even at iodide intake levels below 75 µg/day (Figure A-54 of USEPA 2017; reproduced in Figure 5a). USEPA (2017) used data on the relationship between thyroidal iodide stores (mg) and iodine intake from Delange (2000), which assumes depletion of fT4 at iodide intake levels below 100 µg/day. As is clear from Figure 5b, this assumed model behavior at concentrations below 100 µg/day, which drives model predictions at low intakes, is inconsistent with the NHANES data and could result in overprediction of fT4 responses at moderately low intakes of iodide, including the ranges simulated in the USEPA report. This possibility was investigated in this evaluation and the results are discussed in the next section.

Evaluation of BBDR Model Behavior

Comparison to the Steinmaus et al. 2016 Results

In Appendix B of USEPA (2017), a comparison of the predicted changes in both fT4 and TSH from the BBDR model were compared to the results reported by Steinmaus et al. (2016). The Steinmaus et al. (2016) study was conducted to evaluate the potential for perchlorate exposure to impact thyroid hormone levels in pregnant women (any trimester) in San Diego. They reported an effect of perchlorate on fT4 levels to be similar among women with both low iodine (<100 µg/day) and normal (100-300 µg/day), with a greater effect of perchlorate observed among pregnant women in the high iodine intake group (>300 µg/day). They further noted that this result is in contrast to some previous results from NHANES (Blount et al. 2006) and may be due to the overall iodine sufficiency in the studied population or the fairly long time between urine iodine and serum thyroid hormone sample collection (about 9 weeks).

The comparison of the predicted fT4 changes from the BBDR model and the Steinmaus et al. (2016) results associated with changes in perchlorate dose are reported in Figure B-1 of Appendix B of USEPA (2017) and reproduced in Figure 6. This comparison, which we were able to reproduce using the

366 USEPA (2017) BBDR model, clearly highlights the differences between the model predictions and the
367 published human data. The USEPA (2017) BBDR model simulations with normal iodine intake (170
368 µg/day) demonstrate no change in fT4, which is consistent with other studies in which no impact on
369 fT4 has been observed at doses up to 7 µg/kg/day perchlorate (Greer et al. 2002; Braverman et al.
370 2006). The USEPA (2017) BBDR model greatly under-predicts the changes in fT4, even in the
371 scenario with low dietary iodine intake (75 µg/day), in comparison to the changes reported by
372 Steinmaus et al. (2016). This discrepancy raises concerns about the ability of the USEPA (2017)
373 BBDR model to predict changes in fT4 associated with chronic perchlorate exposure during pregnancy.

374

375 *Greer et al. 2002 – 14 day human controlled perchlorate dosing study*

376 The Greer et al. (2002) study was conducted to establish the dose-response in humans for perchlorate
377 inhibition of thyroidal iodide uptake and any short-term effects on thyroid hormones following
378 exposure for male and female volunteers to perchlorate in drinking water at doses of 7, 20, 100 or
379 500 µg/kg/day for 14 days. The results of this study have previously been relied upon by the USEPA
380 (2005) to derive a reference dose (RfD) and to determine health reference levels (HRLs). The results
381 of this study indicate a decrease in iodide uptake following exposure to a dose of 20 µg/kg/day, but no
382 effect on hormone levels, including fT4 and TSH, at the highest dose tested. A No Observed Effect
383 Level (NOEL) of 7 µg/kg/day was determined based on these results, and an RfD of 0.7 µg/kg/day
384 was adopted, based on NAS recommendations, with the application of an uncertainty factor of 10 for
385 intraspecies variability or sensitive subpopulations.

386 Consistent with the results of the study, our simulations of the adult exposures reported in Greer et al.
387 (2002) with the BBDR model (Table 1) indicated no significant change in fT4 at doses up to 500
388 µg/kg/day. However, predicted concentrations of fT4 are lower than those measured by Greer et al.
389 (2002). The model simulation reported in Table 1 was run with an iodine intake of 90 µg/day, as this
390 was the value USEPA (2017) used in the Greer_test.m script provided with the BBDR model code.
391 However, 90 µg/day is not consistent with the 170 µg/day value USEPA (2017) reports as
392 representing a sufficient intake and USEPA's (2017) documentation does not indicate why a lower
393 value was used for the individuals in the Greer study. Simulation of iodide uptake inhibition (RAIU)
394 appears to over-predict the reduction in uptake compared to measured values, though the qualitative

increasing trend of inhibition with dose behaves appropriately. This discrepancy may result from the low iodine intake chosen by USEPA (2017), or a number of other decisions made in the model revisions, including the reduced Km parameter value. It is unclear why the parameters governing iodide inhibition were altered from previous models that successfully predicted inhibition of iodide in human subjects (Clewell et al. 2007; Merrill et al. 2003; Lumen et al. 2013). Given that iodide inhibition is the obligatory precursor to all downstream effects in the USEPA's proposed mode of action for perchlorate, it would be expected that any changes to the model that lead to reduced accuracy in the prediction of iodide inhibition would be accompanied by substantial support. However, no such support is provided in USEPA (2017) for the changes in the key parameters and the resulting effect on iodide inhibition predictions.

Table 1. Simulation of the Greer et al. (2002) Perchlorate Study

Dose	RAIU (%)		fT4 (pM)	
(µg/kg/d)	Simulated	Measured	Simulated	Measured
0	100	100	10.33	-
7	89	98.2	10.33	-
20	74	83.6	10.32	16.09
100	37	55.3	10.31	15.26
500	11	32.9	10.30	15.44

Braverman et al. 2006 – 6 month human controlled perchlorate dosing study

The Braverman et al. (2006) study was conducted to determine whether prolonged exposure (6 months) of adults to low levels of perchlorate (0.5, 1.0 or 3.0 mg/day) would perturb thyroid function. The study included a small number of individuals (n=13); however, iodine levels were comparable with those of the general population. The authors noted the limitations of the small sample size, but concluded that the results suggested that healthy, euthyroid individuals, with normal levels of iodine intake, can tolerate chronic exposure to perchlorate at doses of up to 3 mg/day (approximately 40 µg/kg/day) without any effects on thyroid function, including inhibition of iodine uptake.

The Braverman et al. (2006) study was simulated as part of the current evaluation using the BBDR model and predicted T3 and TSH levels were compared to the reported measurements (Table 2). fT4

was not compared because it was not clear how to convert the T4 index reported in the study to a concentration and vice versa. As with the Greer et al. (2002) simulation, 90 µg/day was used for iodine intake. Baseline T3 and TSH are similar to the measured values. But, as was seen with fT4, the model fails to predict the observed changes in hormone levels in the adult subjects.

Table 2. Simulation of Braverman et al. (2006) perchlorate study.

Dose	T3 (nM)		TSH (mIU/L)	
(µg/kg/d)	Simulated	Measured	Simulated	Measured
0	2.63	2.49	1.51	1.20
7	2.63	2.51	1.52	1.60
43	2.62	1.77	1.53	2.60

Téllez Téllez et al. 2005a, 2005b – Chilean epidemiological study in pregnant women

Téllez Téllez et al. (2005a, 2005b) reports the results of a longitudinal epidemiological study among pregnant women from three cities in Chile exposed to concentrations of perchlorate as high as 114 µg/L in the public drinking water. The focus of the study was to evaluate maternal thyroid function during pregnancy, neonatal thyroid function and developmental status at birth, and breast milk iodine and perchlorate levels during lactation. The National Academy of Sciences (2005) has reviewed this study in the context of health implications for perchlorate ingestion and concluded this study should be considered in the evaluation of the US experience with perchlorate in drinking water. The total iodine nutrition among this cohort was also noted to be similar to that of US pregnant women (Téllez Téllez et al. 2005a); therefore, this study should be a key consideration in evaluating the relationship between perchlorate exposure, changes in fT4 in pregnant women and developmental status; however, it was not considered in Stage 2 of the USEPA (2017) assessment because it pre-dated the cutoff used by USEPA in their review (2010).

Results from this study indicated no effect on thyroid levels in early pregnancy, late pregnancy, or neonates at birth related to perchlorate in drinking water at concentrations up to 114 µg/L. Given these findings, this study provides a reasonable dataset for validating the impact of high perchlorate exposure concentrations in drinking water on potential changes in fT4 or TSH.

We also ran the (USEPA 2017) BBDR model to simulate the Téllez Téllez et al. (2005a, 2005b) drinking water study (Table 3). The BBDR model predictions of fT4 for GW 13-16 are consistent with the negative results of the study, though the predicted concentrations are lower than those observed. This is not a strong validation of the model given the weak trend of changes in hormone levels seen in comparisons to other studies.

Table 3. Simulation of the Téllez Téllez **et al. 2005a, 2005b study of pregnant women exposed to perchlorate via drinking water.**

Dose	**fT4 (pM)**	
(µg/kg/d)	**Simulated**	**Measured**
0.01	9.74	12.5
0.08	9.73	12.2
2	9.69	12.7

Summary: Evaluation of Model Behavior

Our simulations of the Greer et al. (2002) and Braverman et al. (2006) studies with the BBDR model indicate that thyroid hormone levels are relatively insensitive to inhibition of thyroid iodine uptake by perchlorate exposures as high as 7 µg/kg/day. Moreover, our simulations of the Téllez Téllez et al. (2005a, 2005b) study with the BBDR model do not predict an effect on fT4 from exposures to perchlorate at up to 2 µg/kg/d, consistent with the fact that the exposures were demonstrated to be without effect to pregnant women in the study. However, the USEPA (2017) BBDR modeling analysis (Table 4, taken from USEPA 2017)predicted population-level changes in fT4 deficiency during the first trimester at perchlorate exposures nearly an order of magnitude lower (0.3 µg/kg/d) . This discrepancy suggests that the metric used in the USEPA (2017) approach to assess population-level effects of perchlorate, i.e., a 1% or 5% increase the proportion of thyroxinemic mothers in early pregnancy assuming that all individuals have a low (75 µg/day) iodine intake and an inadequate TSH response (pTSH = 0.398 vs. 1), may be overly conservative.

Table 4. Summary of Results for the Amount of Perchlorate Needed to Increase the Proportion of Hypothyroxinemic, Low Iodine Individuals by a Defined Percentage (with hypothyroxinemia defined as fT4< 10th Percentile) (USEPA 2017)

Gestational Week	fT4 (pmol/L) at the Hypothyroxinemic Cut Point (i.e. 10th Percentile of 170 µg/day Iodine Intake Group) (Column 1)	Corresponding Percentile in 75 µg/day Iodine Intake Group (Column 2)[a]	Perchlorate Dose (µg/kg/day) Associated with a 1 Percent Increase in Proportion Hypothyroxinemic (Column 3)[a]	Perchlorate Dose (µg/kg/day) Associated with a 5 Percent Increase in Proportion Hypothyroxinemic (Column 4)[a]
12	8.80	48.4	0.4	2.2
13	8.78	47.9	0.4	2.2
16	8.63	52.6	0.3	2.1

[a] Results based on central effect estimates, pTSH in BBDR model set to 0.398

457

458 ***Evaluation of the effect of model assumptions on predicted PODs***

459 In order to assess the potential quantitative impact of some of the uncertainties in the BBDR
460 model, we compared model predictions of percent change in fT4 and TSH for a range of
461 perchlorate concentrations using two alternative parameterizations: (1) the parameterization
462 used by the USEPA (2017) to generate their Table 3, and (2) replacing the equation for
463 HCGREG with the equation for VCHNG (in order to provide an appropriately coupled response
464 to hCG stimulation of thyroidal iodine uptake and thyroid hormone production), and also
465 setting pTSH = 1 (the nominal value, as opposed to the lower-bound value of 0.398 used by
466 the USEPA). The simulations (Table 5) were performed with the model calibrated to either the
467 median population thyroid hormone levels (using the script medset.r) or a low (thyroxinemic)
468 population defined as fT4 < 10th percentile (using the script lowset.r). When predicting the
469 effect of perchlorate exposure on fT4 for the median population there is not a significant
470 difference between the USEPA results and the alternative parameterization; however, the
471 USEPA model parameterization results in more than a factor of 2 greater sensitivity of TSH
472 levels to perchlorate compared to the alternative parameterization. This difference is primarily

473 due to the change in pTSH. On the other hand, when predicting the effect of perchlorate
474 exposure on hypothyroxemic individuals, both fT4 and TSH responses to perchlorate exposure
475 are significantly lower using the alternative parameterization. Thus, the parameters that were
476 altered in the recent revision of the model (VCHNG, HCGreg, pTSH, KmNiS_p) increase the
477 predicted effect on thyroid hormone levels compared to the expected response with the well-
478 validated precursor event of iodide inhibition. The sensitivity of the prediction to changes in
479 these parameters, and the disconnect between the prediction of iodide inhibition and thyroid
480 hormone levels, calls for better justification – and evaluation – of the given parameter values.

Table 5. Predicted fT4 and TSH Concentrations at Various Doses of Perchlorate for 75 µg/day Iodine Intake

Perchlorate Dose (µg/kg/day)	fT4 (pmol/L) (% Change from 0 Dose)				TSH (mIU/L) (% Change from 0 Dose)			
		USEPA[0]	VCHNG + pTSH[1]	VCHNG + pTSH[1]		USEPA[0]	VCHNG + pTSH[1]	VCHNG + pTSH[1]
	Population	Median	Median	Low	Population	Median	Median	Low
0	Absolute	8.6	9.9	7.5	Absolute	2.2	1.5	3.0
1		-0.74	-0.8	-0.31		3.3	1.4	1.9
2		-1.5	-1.6	-0.61		6.6	2.7	3.8
3	Percent	-2.1	-2.3	-0.9	Percent	10	4.1	5.7
4	Change	-2.8	-2.9	-1.2	Change	14	5.5	5.7
5		-3.4	-3.5	-1.5		17	6.9	7.7
10		-6.2	-6.2	-2.8		36	14	19

[0] Results using pTSH = 0.398

[1] Results using HCGREG replaced with VCHNG, and pTSH=1

481 **Review of Literature Linking BBDR Results to Neurodevelopment Outcomes**

482 Chapter 5 of USEPA (2017) focuses on the SAB's recommendation to "Identify literature and conduct
483 analyses to support the model outputs for the downstream steps" from the BBDR's predicted changes
484 in thyroid hormones following exposure to perchlorate. Specifically, Chapter 5 was developed to
485 present the process USEPA (2017) used to identify literature to support the draft approach for
486 derivation of the MCLG for perchlorate. USEPA (2017) states, "Based on the recommendations of

487 previous peer review panels, USEPA assumed that changes in thyroid hormone levels would be
488 expected to lead to neurodevelopmental outcomes", and because of this assumption, a complete
489 systematic review of the body of literature on this topic was not performed. Instead, a "focused
490 review of the published literature" was conducted.

491 The approach is inconsistent with recent recommendations from the National Research Council (NRC
492 2014) regarding systematic review and evidence integration. These recommendations are currently
493 being incorporated into the USEPA's Integrated Risk Information System (IRIS) process and USEPA
494 has recently released scoping and problem formulation materials for several new Integrated Risk
495 Information System (IRIS) assessments, including ethylbenzene (USEPA 2014a), and naphthalene
496 (USEPA 2014b). The approach applied in these assessments is intended to follow recommendations
497 provided by the National Research Council (NRC 2013). While development of MCLGs are not part of
498 the IRIS process, the application of systematic review principles in the identification of studies to
499 define the relationship between fT4 and neurodevelopmental effects, is needed. The application of
500 these principles would not only assist in defining the highest quality studies to address a specific
501 research question, they also provide a way to integrate all of the available evidence for the specific
502 research questions raised by the SAB. Systematic reviews include the formulation of a specific
503 question to be addressed and developing a protocol that specifies the methods that will be used to
504 address the question. While a broad research question can lead to a large systematic review, if the
505 research question is limited, such as in the case of perchlorate, then the systematic review becomes
506 more focused.

507 For the USEPA (2017) draft MCLG approach, a systematic review question could have been easily
508 developed based on the SAB recommendation (i.e. "Identify literature and conduct analyses to support
509 the model outputs for the downstream steps") and the protocol would simply be focused on the
510 methods for conducting the systematic review to address this very focused systematic review question
511 in a transparent manner. Transparency being defined by USEPA as "sufficient information will be
512 available to understand the scientific rational behind decisions, as well as, reproduce methods used to
513 identify and evaluate data". However, in the case of the literature identified for consideration in the
514 draft MCLG approach for perchlorate, a well-defined protocol for all steps of the process has not been
515 developed and therefore is inconsistent with the recommendations of the NRC (2013):

> *"A priori decisions and a predefined protocol are critical during the systematic review process (Berlin and Colditz 1999; Dickersin 2002); the protocol should describe the following steps: the research question, the search strategy and data sources, the study inclusion and exclusion criteria, the data to be abstracted and derived from the original studies (such as sample size, exposure and outcome assessment methods, and confounders evaluated), the criteria and methods for pooling effect estimates and measures of variability among studies. Systematic reviews and meta-analyses need to be replicable; other investigators following the same steps should be able to identify the same articles, abstract the same data, and reach similar conclusions."*

At each step of the process for identifying studies for use in the development of the MCLG approach for perchlorate, a detailed set of criteria is needed. For example, if decisions are made to include or exclude any studies, there should be very detailed criteria indicating why studies were included or excluded and it should be specified prior to the initiation of the literature searching process. The criteria for each step should be described in such a way that an independent reviewer could use it to replicate the results of the literature search and review; however, there are several areas in the USEPA (2017) draft MCLG approach for perchlorate where this level of detail is lacking, making it difficult for an independent reviewer to replicate the results.

Systematic Review Research Questions

An overall hypothesis or systematic review research question should be developed that is based on the SAB recommendation to clarify the focus of the review and the linkage between altered maternal fT4 (as predicted by the BBDR model) and the potential for adverse neurodevelopmental effects in offspring. Some additional explanation as to how USEPA arrived at the specific neurodevelopmental outcomes of concern should be provided.

Searching the Published Literature

While the literature search key words are presented in the USEPA (2017) report, there is a lack of explanation as to the reasoning behind the focus on the outcome of concern. The research question should be used to develop the literature search. The major points used or considered in developing

544 the literature search strategy should be presented. In addition, there should be a detailed explanation
545 of the criteria used to screen the literature search results. Furthermore, USEPA (2017) does not
546 report the details of the literature search results. For each search string reported in Table 9 of the
547 USEPA (2017) report, a total number of citations identified should be reported. In addition, the
548 criteria used to screen the original search results should be clearly reported in the document.
549 Essentially, each step of the literature search and review should be reported in such a way that any
550 independent party could easily reproduce the results reported in Chapter 5 of USEPA (2017). The lack
551 of this type of information does not allow the reader to determine if any key studies may have been
552 removed from consideration.

553 *Literature Screening Approach and Selection of Key Studies*

554 USEPA (2017) states that a 3 step approach was used to identify studies for consideration in the
555 development of the approach for derivation of the MCLG for perchlorate. The approaches utilized by
556 USEPA (2017) to identify the epidemiological studies for this evaluation were strictly focused on the
557 appropriateness of the quantitative data for consideration in combination with the output of the BBDR
558 model. Group 2 (studies with categorical analyses only) and Group 3 (studies with analyses not
559 directly compatible with BBDR output) studies were apparently eliminated from consideration in the
560 assessment. While not directly compatible with BBDR modeling output, it is possible that these
561 studies may provide information important in understanding the potential relationship between
562 changes in thyroid hormones and the potential for neurodevelopmental effects, as well as potential
563 key confounders.

564 While 15 studies were identified in Group 1, only 5 of these were determined by USEPA to include
565 analyses that could be used to connect the results of the BBDR model to incremental changes in
566 adverse neurodevelopmental effects. A clearly defined set of inclusion and exclusion criteria should be
567 provided to clearly convey to the reader why the other 40 studies in Groups 1, 2, and 3 were not
568 considered. In addition, studies that provide no evidence of an inverse relationship between
569 perchlorate exposure and serum thyroid function (e.g. Ghassabian et al. 2014; Modesto et al. 2015;
570 Moleti et al. 2016; Noten et al. 2015) should also be considered to not only understand why these
571 results are in contrast to the potential research question, but also that the overall weight of evidence
572 can be determined. It is possible that the majority of studies provide evidence that critical factors that

573 are not reported in some of the available studies may explain the reported changes in serum thyroid
574 function.

575 *Assessment of Study Quality and Risk of Bias*

576 According to recent recommendations from the National Research Council (NRC 2014), the National
577 Toxicology Program's (NTP) Office of Health Assessment and Translation (OHAT) method for the
578 assessment of study quality and risk of bias of the literature (NTP 2015) is one method that should be
579 considered for qualitative and quantitative assessments. "An assessment of study quality evaluates
580 the extent to which the researchers conducted their research to the highest possible standards and
581 how a study is reported. Risk of bias is related to the internal validity of a study and reflects study-
582 design characteristics that can introduce a systematic error (or deviation from the true effect) that
583 might affect the magnitude and even the direction of the apparent effect" (NRC 2014). Each study
584 meeting inclusion criteria in Group 1, 2, and 3, should be evaluated against a predetermined set of
585 study quality and risk of bias criteria and the results of this evaluation should be presented in the
586 perchlorate MCLG approach report.

587 Uncertainties Critical to Characterizing Changes in Thyroid Hormone Levels in Pregnant Women
588 Associated with Neurodevelopmental Changes in Offspring

589 The draft MCLG approach presented in USEPA (2017) to predict doses of perchlorate that would result
590 in per unit changes in neurodevelopmental measures, is, as noted by USEPA (2017), "…dependent
591 upon predictions from the BBDR model, the derivation of the distribution of fT4, and the evaluations of
592 the relationship between fT4 and neurodevelopment. Each of these steps has inherent uncertainties
593 associated with it."

594 A major source of uncertainty is related to the five studies in Group 1 with data that could be used to
595 quantitatively describe the relationship between thyroid hormone levels in early pregnancy and
596 changes in neurodevelopment (Pop et al. 1999, 2003; Finken et al. 2013; Korevaar et al. 2016;
597 Vermiglio et al. 2004). None of these five studies relied upon data from US populations or have been
598 demonstrated to have iodine intake similar to US populations. Yet according to the American Thyroid
599 Association (Alexander et al. 2017), the reference range of both TSH and fT4 in pregnant women
600 varies depending upon ethnicity. While two studies in Group 1 focused on population groups within

601 the United States, neither were considered for the model because T4 and not fT4 was measured in the
602 pregnant females (Oken et al. 2009) and the relationship between fT4 and neurodevelopment was
603 evaluated in late pregnancy and did not reach statistical significance (Chevrier et al. 2011). USEPA
604 (2017) (Section 6.5.1) states "there is no reason to believe that the impact of fT4 on
605 neurodevelopment would differ by country, unless there is a substantial difference in iodine intake".
606 While USEPA (2017) does make an effort to evaluate changes in iodine intake in women from various
607 populations, including the US, there are not substantial data reported in the peer-reviewed literature
608 to validate the conclusions that the impact of fT4 on neurodevelopment would differ by population or
609 uncertainty in iodine intake levels would have an impact on the derivation of the MCLG. This is
610 inconsistent with data from the American Thyroid Association (Alexander et al. 2017) that suggest
611 variability in the distribution of thyroid hormone levels across populations and even within ethnicities
612 within a single population.

613 USEPA (2017) also notes that all five studies used for quantitative analysis relied on a one-time fT4
614 level during pregnancy (Section 6.5.5). The influence of changes in maternal fT4 on fetal brain
615 development is likely greatest during early pregnancy. The variability in maternal fT4 levels during
616 pregnancy and the lack of measurement of fT4 at time points throughout pregnancy in the studies
617 provides a substantial data gap and lack of information needed to validate some of the assumptions
618 relied upon in the development of the BBDR current model as well as the resulting predictions of the
619 model. As stated in USEPA (2017),

620 *"Circulating T3 and T4 levels in an individual are maintained within a narrow range by*
621 *a negative feedback loop with TSH from the pituitary and TRH from the hypothalamus*
622 *that operates around a "set-point." This set-point is different from individual to*
623 *individual, which generates a population variance in blood levels of thyroid hormone*
624 *that is considerably broader than the individual variance (Andersen, Pedersen, Bruun,*
625 *& Laurberg 2002). Therefore, in euthyroid individuals, serum T4 and T3 fluctuate*
626 *within a fairly narrow range (about 10% of the population variance), maintained by*
627 *the negative feedback relationship with serum TSH from the pituitary gland. This*
628 *normal variation creates a situation where single measures of free or total T4 and TSH*

629 *are a somewhat imprecise measure of an individual's average T4 and TSH*
630 *concentrations (Andersen et al. 2002)."*

631 Several other areas of uncertainty are also highlighted by USEPA (2017). Specifically, USEPA
632 (2017) noted that none of the five studies carried forward provided iodine intake levels
633 (Section 6.5.3), which adds significant uncertainty to the estimates. Three of the 5 studies
634 (Pop et al. 1999, 2003; Vermiglio et al. 2004) also have populations of less than 30
635 decreasing the statistical power of the studies (section 6.5.4) relied upon for establishing the
636 relationship between changes in fT4 and neurodevelopmental changes. USEPA (2017) also
637 noted uncertainties in regard to the analytical methods used to evaluate fT4 levels and while
638 approaches are being introduced to standardize analytical methods, results at different time
639 points and from different countries may vary considerably due to differences in analytical
640 procedures (USEPA 2017). USEPA (2017) also notes that "there is uncertainty regarding the
641 true fT4 levels at various percentiles in the distribution around the median output from the
642 BBDR model. This is exemplified by the fact that in this analysis larger unit changes are being
643 seen with increasing percentiles of fT4 in most analyses." Finally, other confounders such as
644 iron deficiency were not considered in the analysis. Iron deficiency in pregnant mothers,
645 which is noted in approximately 18% of pregnant women in the US (Cantor et al. 2015), may
646 also be associated with hypothyroxinemia (Yu et al. 2015) and failing to directly account for a
647 relationship between iron deficiency and hypothyroxinemia may introduce an uncertainty into
648 this analysis.

649 While all these uncertainties are noted by USEPA (2017), there is no attempt to adjust the
650 draft MCLG approach in any way to account for these uncertainties. Many of these, especially
651 confounders such as iron deficiency in the study population and a lack of information on iodide
652 intake, can have a significant effect in characterizing changes in thyroid hormone levels
653 associated with changes in neurodevelopmental outcomes. In the absence of adequately
654 accounting for these uncertainties, it is difficult to have confidence that BBDR model
655 predictions of small changes in a specific thyroid hormone (e.g. fT4) may accurately predict
656 the potential for neurodevelopmental effects.

The inadequacy of the USEPA (2017) literature review is substantiated by the comments of the External Peer Review for USEPA's Proposed Approaches to Inform the Derivation of a Maximum Contaminant Level Goal for Perchlorate in Drinking Water (Versar 2018). Comments regarding the USEPA (2017) literature search included:

- "The literature search produced ten studies (that assessed maternal serum FT4 concentrations as a continuous measure which did not observe an adverse effect on offspring neurocognition), as well as those in Group 2 that assessed serum FT4 as categorical measures. Although their inclusion may not necessarily be recommended in the final model, comparison of the estimated effects on the various neurocognitive outcomes with and without these may indeed inform the degree of uncertainty inherent in the present model. Several of the studies in Group 2 were able to demonstrate significant adverse outcomes (Berbel 2009 as one excellent example), and also their more global nature would help support the generalizability of the present model."
- "Excluding these studies lessens the power of the total sample size and thus the ability to detect an association between maternal hypothyroxinemia and any of the offspring outcomes, but provides what may be a somewhat exaggerated estimate of the potential adverse effects of perchlorate exposure. This approach is more conservative, to which there are pros and cons of doing so, toward derivation of a perchlorate MCLG. With this approach, the goal is to minimize exposure to the lowest perchlorate concentration associated with any number of adverse outcomes. I would favor the more liberal public health approach, which is inclusion of all available studies, whether they are positive or negative. Although the perchlorate MCLG may be higher, this latter approach would be consistent with using all available evidence to improve the scientific rigor of the proposed study question."

The peer reviewers also suggested a number of additional peer-reviewed studies that they felt should have been considered to inform BBDR modeling of the quantitative relationship between thyroid hormone levels and neurodevelopmental outcomes:

- Bárez-López S, Jesus-Obregon M, Bernal J, Guadaño-Ferraz A. 2017. Thyroid Hormone Economy in the Perinatal Mouse Brain: Implications for Cerebral Cortex Development. Cerebral Cortex, 28(5): 1783-1793.
- Bath S, Steer C, Golding J, Emmett P, Raymen M. 2013. Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC). The Lancet, 382(9889): 331-337.
- Bernal J. 2017. Thyroid hormone regulated genes in cerebral cortex development. Journal of Endocrinology, 232(2): R83-R97.
- Casey B, Thom E. 2017. Subclinical Hypothyroidism or Hypothyroxinemia in Pregnancy. The New England Journal of Medicine, 377(7): 701.
- Casey B, Thom E, Peacemann A, Varner M, Sorokin Y, Hirtz D, Reddy U, Wapner R, Thorp J, Saade G, Tita A, Rouse D, Sibai B, Iams J, Mercer B, Tolosa J, Caritis S, VanDorsten JP. 2017. Treatment of Subclinical Hypothyroidism or Hypothyroxinemia in Pregnancy. The New England Journal of Medicine, 376: 815-825.
- Endendijk J, Wijnen H, Pop V, van Baar A. 2017. Maternal thyroid hormone trajectories during pregnancy and child behavioral problems. Hormones and Behavior, 94: 84-92.
- Hales C, Taylor P, Channon S, Paradice R, McEwan K, Zhang L, Gyedu M, Bakhsh O, Muller I, Draman M, Gregory J, Dayan J, Rees D, Ludgate M. 2018. Controlled Antenatal Thyroid Screening II: effect of treating maternal sub-optimal thyroid function on childhood cognition. The Journal of Clinical Endocrinology and Metabolism, 103(4): 1583-1591.
- Lazarus J, Bestwick J, Channon S, Paradice R, Maina A, Rees R, Chiusano E, John R, Guaraldo V, George L, Perona M, Dall'Amico D, Parkes A, Joomun M, Wald NJ. 2012. Antenatal Thyroid Screening and Childhood Cognitive Function. The New England Journal of Medicine, 366: 493-501.
- Taylor PN, Okosieme OE, Murphy R, Hales C, Chiusano E, Maina A, Joomun M, Bestwick JP, Smyth P, Paradice R, Channon S, Braverman LE, Dayan CM, Lazarus JH, Pearce EN. 2014. Maternal Perchlorate Levels in Women with Borderline Thyroid

Function During Pregnancy and the Cognitive Development of Their Offspring: Data from the Controlled Antenatal Thyroid Study. The Journal of Clinical Endocrinology & Metabolism, 99(11): 4291-4298.

In the draft MCLG approach, USEPA (2017) focused on five studies that evaluated the relationship of maternal fT4 and several neurodevelopmental endpoints (IQ, mental development index (MDI), psychomotor development index (PDI), standard deviation of reaction time), based on measurements of fT4 during early pregnancy. Results from previous studies have provided the basis for No Observed Effect Levels (NOELs) for health effects of perchlorate in the development of Reference Doses and currently recommended Health Reference Levels (HRLs), including Greer et al. (2002) in which adult men and women were exposed to perchlorate in drinking water at doses of 0.007, 0.02, 0.1, or 0.5 mg/kg/day for 14 days demonstrated a NOEL for perchlorate inhibition of radioiodide uptake by the thyroid NIS following exposure to 7 µg/kg/day. The point of departure from the Greer et al. (2002) study represents a perchlorate level that precedes the inhibition of iodine uptake by the thyroid. The NAS RfD developed based on the point of departure (POD) from this study is a deviation from the Agency's traditional approach of using a No Observed Adverse Effect Level (NOAEL) for regulatory actions. The NAS's use of a No Observed Effect Level (NOEL) is based on "using a nonadverse effect that is upstream of the adverse effect [which] is a more conservative and health protective approach".

While these studies have not been conducted in pregnant women (the population of interest for the draft MCLG approach), as noted by in USEPA (2017):

> *"…the BBDR model predicts very little difference in non-pregnant and first-trimester response to perchlorate. This likely occurs because the half-life of (organified) iodine in the adult thyroid is around six months, hence the availability of thyroidal iodine in the first trimester pregnant woman is determined to a very large extent by her nutrition and perchlorate exposure several years preceding pregnancy."*

This suggests that a comparison of the current modeling results to those from studies conducted in adults should provide insight into the predictions of the model and the conclusions regarding the changes in thyroid hormone levels that may result in neurodevelopmental effects.

742 The current draft approach for deriving the MCLG assumes any exposure to perchlorate reduces fT4 to
743 some extent (p. 3-17 of USEPA 2017). In addition, linear regression analyses conducted to evaluate
744 the relationship between changes in fT4 and neurodevelopmental effects further assumes any change
745 in fT4 results in some risk of neurodevelopmental effects. These assumptions are in contrast to the
746 results from Greer et al. (2002) in which exposures to perchlorate were as high as 500 µg/kg/day and
747 no impact on thyroid hormone levels was observed. This was true for both men and women. In
748 addition, in a study conducted by Braverman et al. (2006), 6 months of exposure to perchlorate in
749 capsules at doses up to 3 mg/day (approximately 40 µg/kg/day) was reported to have no effect on
750 thyroid function, including inhibition of thyroid iodide uptake as well as serum levels of thyroid
751 hormones, TSH, and Tg in a small group of volunteers.

752 USEPA (2017) notes (p. 6-16) that from results of the literature review, it appears the relationship
753 between maternal fT4 and fetal brain development has a temporal relationship, with this influence
754 likely being greatest in early pregnancy (i.e. prior to mid-gestation). The focus of the evaluation is on
755 gestational weeks 12, 13, and 16, where the mother's fT4 levels will have the greatest impact on the
756 fetus. This should allow for comparison to the model results in pregnant women to results from
757 previous studies focused on identification of perchlorate concentrations that would impact fT4 levels in
758 adult women, such as the Greer et al. (2002) study.

759 Based on the BBDR model predictions, USEPA (2017) estimates that a perchlorate dose of 0.3-0.4
760 µg/kg/day would result in a 1% increase in the proportion of the population with hypothyroxinemia
761 and a perchlorate dose of 2.1-2.2 µg/kg/day would result in a 5% increase in proportion of the
762 population with hypothyroxinemia. These modeling results suggest a potential for a significant change
763 in thyroid hormones, as well as adverse effects on neurodevelopment at doses of perchlorate exposure
764 for which there is evidence that decreases in fT4 are not observed. Based on the mode of action
765 proposed by USEPA (2017), decreases in fT4 and increases in TSH would be prerequisite steps for the
766 potential for neurodevelopmental effects. These changes in hormone levels are not observed in the
767 Greer et al. (2002) study following exposure up to 500 µg/kg/day. The draft MCLG approach suggests
768 population changes in fT4 would be observed that would shift the proportion of pregnant women that
769 would be hypothyroxinemic at doses of perchlorate below the previously defined NOEL (7 µg/kg/day).

Table 6 (Table 39 of USEPA 2017) provides the predicted dose of perchlorate per unit change in neurodevelopmental measure for low iodine intake individuals. Those for IQ are approximately at or above (6.5 – 45 µg/kg/day) the NOEL from Greer et al. (2002) and are associated with decreases in fT4 of 4.3 to 18.7%. The doses associated with other neurodevelopmental endpoints are 1.7 to 3.0 µg/kg/day and are associated with decreases in fT4 of 1.3 to 2.4%. These percent changes in fT4 are very small and considering the potential uncertainty and variability in measuring fT4 levels, there is a lack of evidence that such small changes in fT4 will result in clinical observations. Reference ranges for fT4 are 0.9 – 2.5 ng/dL in infants (0-5 days) and 0.9 – 1.7 ng/dL in adults (> 20 yrs) (https://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/8725). Thus, for an adult, at the low end of the reference range, we would expect a change from 0.900 to 0.878 ng/dL, a value that given the number of significant figures in the reference value would not be measurable. The dose of perchlorate estimated to result in a 1% or 5% increase in the proportion of hypothyroxinemic pregnant women is even lower, ranging from 0.3 to 2.2 µg/kg/day. USEPA (2017) findings are contrary to multiple studies in adults and pregnant women (Greer et al. 2002; Braverman et al. 2006; Téllez Téllez et al. 2005a, 2005b) provide robust evidence that no impact on iodine uptake or thyroid hormone levels would be expected at these dose levels. Based on the mode of action proposed by USEPA (2017), these precursor impacts are necessary to generate the neurodevelopmental effects derived from the BBDR model.

Table 6. Predicted Dose of Perchlorate per Unit Change in Neurodevelopmental Measure for Low Iodine Intake Individuals based on Central Effect Estimates at the Median fT4 level (USEPA 2017)

Study	Endpoint	ΔfT4 in pmol/L (% ΔfT4 from 0 dose perchlorate, iodine intake = 75 µg/day)	Dose of perchlorate per unit change in endpoint (µg/kg/day)[a]
Korevaar et al. (2016) Quadratic	IQ	-1.08 (12.2%)	23
Korevaar et al. (2016) USEPA Independent Analysis: Bivariate	IQ	-0.98 (11.1%)	20
Korevaar et al. (2016) USEPA Independent Analysis: Multivariate	IQ	-1.66 (18.7%)	45
Vermiglio et al. (2004)	IQ	-0.37 (4.3%)	6.5
Pop et al. (2003)	MDI	-0.15 (1.7%)	2.2
Pop et al. (2003)	PDI	-0.12 (1.3%)	1.7
Pop et al. (1999)	PDI	-0.12 (1.3%)	1.7
Finken et al. (2013)	SD of Reaction Time	-0.21 (2.4%)	3.0
BBDR model (USEPA 2017)	1% or 5% increase in proportion of hypothyroxinemic pregnant women[b]	1% or 5%	0.3 – 0.4[c] [1%] 2.1 – 2.2[c] [5%]

[a] Based on the regression analysis for the range of fT4 data within each study. Central beta estimates of the low iodide intake population (= 75 µg/day) are presented.

[b] Hypothyroxinemia defined as fT4 < 10th percentile

[c] Range based on gestational week used to perform the analysis (12 to 16 weeks).

788

DISCUSSION

A critical review of the (USEPA) 2017 report entitled "Draft Report: Proposed Approaches to Inform the Derivation of a Maximum Contaminant Level Goal for Perchlorate in Drinking Water", as well as the BBDR model that was proposed for use in derivation of the MCLG, was conducted. Overall, conducting this review and assessment of the BBDR model was beset by multiple challenges and the effort highlighted a number of uncertainties in the use of the model. The main challenges that the review presented were due to the complexity of the BBDR model itself. The co-authors of this review, who are widely considered to be experts in the area of PBPK and BBDR model development, found it difficult to evaluate the complex interactions of model parameters and their relationship to the predictions of the model. In our efforts to reproduce simulations provided in USEPA (2017), it was noted that instructions for running the model for different scenarios, and documentation of the rationale for the model parameter values associated with them, were sometimes inadequate; this deficiency, which is inevitable in a complex model, was exacerbated by the number of code scripts required to set the parameters used to generate the various results in the document. As a result, the ability to independently verify all aspects of the model were impeded by uncertainties associated with the steps necessary to reproduce figures and tables in the report, or to perform comparisons of model predictions to data for alternative exposure scenarios or studies.

As suggested by C.A.R. Hoare in his 1980 ACM Turing Award Lecture: "There are two ways of constructing a software design: One way is to make it so simple that there are obviously no deficiencies and the other way is to make it so complicated that there are no obvious deficiencies." By their nature, BBDR models are seldom simple; to the extent that BBDR models attempt to describe complex biological systems they will inherently be difficult to comprehend. The criticisms of the perchlorate PBPK model in this case study are not meant to suggest that the model is incorrect or un-useful, and they should not be taken as criticisms of the utility of BBDR modeling in general. Used appropriately, BBDR models can provide important information for better risk assessment decision-making. The issue that needs to be addressed in each case is whether a BBDR model is fit for the intended purpose of using it in the risk assessment.

The first use of PBPK modeling in risk assessments dates back to the 1980s (USEPA 1987) and yet the application of PBPK modeling to replace default dosimetry remains controversial, primarily due to

818 concerns regarding model uncertainty. To address these concerns, the OMB (2007) memorandum on
819 risk analysis recommended the presentation of results from multiple dose-response approaches to
820 provide a more robust risk characterization. In this scenario, a fit-for-purpose BBDR model can
821 provide information on the most scientifically plausible risk estimate for comparison with the results of
822 default approaches (Clewell et al. 2008). Consistent with this OMB recommendation, one focus of our
823 evaluation was determining how the results of the BBDR modeling could inform the likelihood that the
824 current perchlorate guideline (USEPA 2005), which is based on inhibition of thyroidal iodine uptake in
825 adults, is also protective of concerns regarding neurodevelopmental effects of perchlorate. This
826 question is discussed in the Conclusion.

827 The current BBDR model that was relied upon for the USEPA (2017) draft approach is an extension of
828 previous models that have been validated and published in the peer-reviewed literature (Clewell et al.
829 2007; Merrill et al. 2003; Lumen et al. 2013). Similar values for key parameters have been
830 successfully used across the previous models, yet changes were made in the current model or new
831 parameters added (e.g. VCHNG, HCGreg, pTSH, KmNiS), often with little or no evidence or
832 justification provided to support these revisions in the USEPA (2017) documentation. Additional
833 support for these changes will be needed to provide validation of the current revisions to the BBDR
834 model and to provide confidence in the predictions of changes in fT4 made by the model.

835 Certainly, confidence in the BBDR model predictions is undermined by the model's inability to simulate
836 the results from the Steinmaus et al. (2016) study. In Appendix B of USEPA (2017), a comparison of
837 the predicted changes in both fT4 and TSH from the BBDR model were compared to the results
838 reported by Steinmaus et al. (2016) (reproduced in Figure 6). The Steinmaus et al. (2016) study was
839 conducted to evaluate the potential for perchlorate exposure to impact thyroid hormone levels in
840 pregnant women in San Diego. This comparison clearly highlights the differences between the model
841 predictions and those from a published study. The baseline BBDR simulations with normal iodine
842 intake (170 µg/day) demonstrate no change in fT4, which is consistent with other studies in which no
843 impact on fT4 has been observed at doses up to 7 µg/kg/day (Greer et al. 2002; Braverman et al.
844 2006). The BBDR model underpredicted changes in fT4, even in the scenario with low dietary iodine
845 intake (75 µg/day), when compared to the changes reported by Steinmaus et al. (2016). This
846 discrepancy calls into question the ability of the model to predict changes in fT4 associated with

847 perchlorate exposure. In particular, the proposed MCLG approach depends on model predictions of
848 small changes in fT4 as low as approximately 1% (Table 6) being associated with unit changes in
849 neurodevelopmental endpoints. Predictions of this precision would require a level of model precision
850 that has not been demonstrated by comparisons to existing data.

851 Many of the changes in fT4 that are predicted by the draft MCLG approach to estimate impact on the
852 population distribution of fT4 and therefore result in per unit changes in neurodevelopmental
853 outcomes are small percent changes (some as low as a 1.3-4.3% change). This would appear to
854 suggest that the extended version of the BBDR model has a capability to estimate small changes in
855 fT4 with a level of precision that is not demonstrated by any adequate validation. In fact, BBDR model
856 predictions of fT4 underpredict observed data in human studies (Tables 1 and 3) by as much as 25-
857 35%. Moreover, considering the variability of fT4 in the populations of interest, there is uncertainty as
858 to whether these slight changes could be measured clinically, considering the greater impact of iodine
859 intake on hormone levels. Considering the lack of data to support critical parameters and
860 assumptions in the model, as well as the impact of the variability of iodine intake on model
861 predictions, it seems crucial that validation of the BBDR model by comparison with observed data be
862 used to provide confidence in the predictions of the BBDR model. However, the BBDR model clearly
863 fails the only comparison that has been conducted (Figure 6), with the BBDR model predictions falling
864 outside the bounds of the statistical confidence limits estimated for the Steinmaus et al. (2016)
865 relationship between perchlorate dose and fT4. Each of the components of the BBDR model combined
866 result in compounded uncertainty in the modeling results.

867 Until additional data are available to validate current extensions of the BBDR model to the pregnant
868 woman, the Greer et al. (2002) and Braverman et al. (2006) studies provide the critical information in
869 determining concentrations of perchlorate that do not result in significant inhibition of iodide uptake
870 and, therefore, impacts on fT4. Based on recommendations from the National Academy of Sciences
871 (2005), points of departure provided by these studies used in combination with uncertainty factors
872 were considered to be protective of sensitive subpopulations, this approach has previously been relied
873 upon to support guidelines for perchlorate in drinking water under the Safe Drinking Water Act (USEPA
874 2008), and has also been used more recently by JECFA (2011) and EFSA (2014) in their regulation of
875 perchlorate.

CONCLUSIONS

We applaud the USEPA for the application of a BBDR model in their draft MCLG approaches, as these models integrate the available science for a compound of interest. However, while the hormone component of the model is a scientific improvement in terms of incorporating the available biology, there is a lack of data to provide critical validation in multiple steps of the proposed approach and to support several assumptions/parameters within the BBDR model. In particular, while no major structural defects in the USEPA (2017) BBDR model were identified, there are a number of uncertainties in the model parameterization that call into question its use for predicting very small changes in clinical hormone values, such as a 1% change in fT4 (Tables 4-6) While the model prediction for 1% change in fT4 (0.3-0.4 µg/kg/day) would yield a POD lower than the USEPA (2005) RfD, that level of precision is a not supported by the comparison of the model predictions with available data. Nonetheless, the consistency of the model-predicted PODs based on the epidemiological endpoints (Table 6), and the relationship of these results with previous risk assessments based on biologically sound precursors (iodide inhibition in thyroid), indicate that the interim health standard would be sufficiently protective against the developmental neurological endpoints of concern, as illustrated in Figure 7, which compares the point of departure from the USEPA (2005) IRIS assessment with the PoDs calculated by the BBDR model in the USEPA (2017) report (Table 6). The USEPA (2005) RfD (red bar) is protective for all of the endpoints from epidemiological studies and is consistent with a change in population fT4 levels of less than 5%.

Beginning with the initial risk characterization for perchlorate (USEPA 2002), the fundamental underpinning of the agency's risk assessment approach has been the use of an obligatory precursor as a conservative basis for protecting against downstream health effects. As elaborated in the original documentation (USEPA 2003), the effects of perchlorate are mediated by the inhibition of thyroidal iodine uptake by perchlorate. Unless perchlorate concentrations in the blood are sufficient to disrupt iodine uptake, there is no plausible basis for suggesting an effect of perchlorate on thyroid hormone homeostasis or subsequent events leading to developmental or (in the rat) carcinogenic effects. The recent studies suggesting a relationship between perchlorate exposure and decreased fT4 do not impeach this causal relationship. Therefore, until the significant uncertainties in the current BBDR

model and draft MCLG approaches can be addressed, USEPA should continue to rely on the RfD approach based on inhibition of thyroidal iodine uptake (USEPA (2005), as recommended by the National Academy of Sciences (2005) for any further regulatory action. The USEPA (2005) RfD includes an intraspecies uncertainty factor of 10 "to protect the most sensitive population, the fetuses of pregnant women who might have hypothyroidism or iodide deficiency." None of the predictions of the BBDR model suggest that this uncertainty factor is inadequate.

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1141 Figure 1. Mode-of-action model for perchlorate toxicity proposed by the USEPA (2002).
1142 Inhibition of iodide uptake in the thyroid by perchlorate is an obligatory precursor for all
1143 downstream cancer and noncancer endpoints, including neurodevelopment.

1144 Figure 2: Structure of the Early Pregnancy BBDR (USEPA 2017)

1145 Figure 3: Variation in free T4 (fT4 in early pregnancy (as reported in USEPA 2017))

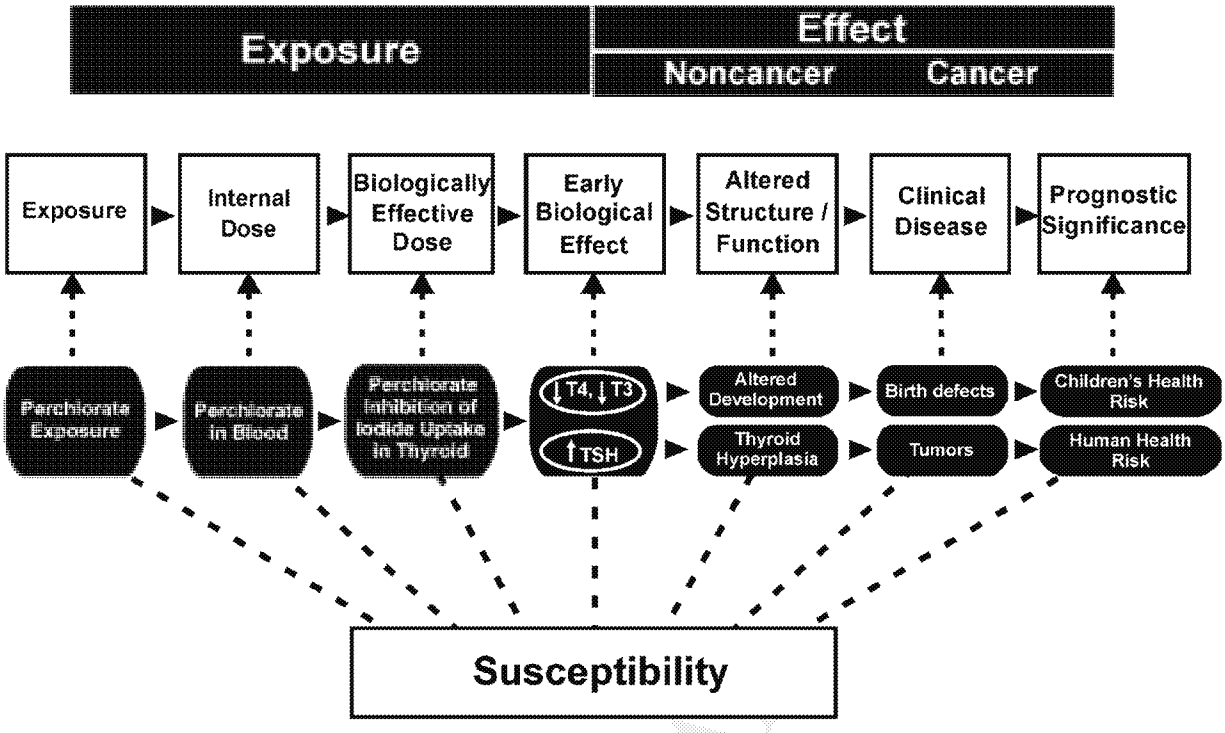
1146 Figure 4, Comparison of parameters controlling hCG-dependent changes in thyroidal uptake
1147 (VCHNG, green) and thyroid hormone production rate (HCGREG, purple) in the BBDR model as
1148 a function of gestational age. Despite the fact that both parameters are dependent upon hCG
1149 levels, the predicted trends across gestation are not consistent.

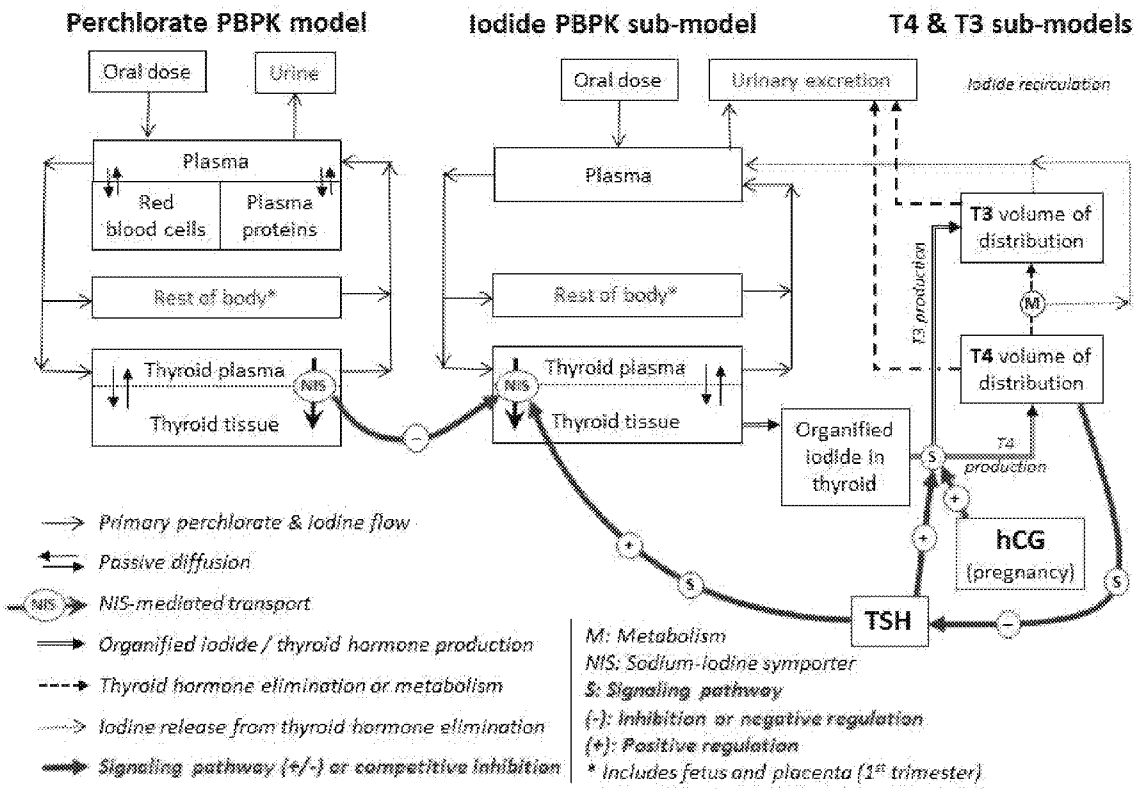
1150 Figure 5. Panel a: Model predictions for free T4 (fT4) in non-pregnant women as a function of
1151 iodine intake compared to data from NHANES 2007-2012 (USEPA 2017). Panel b: Underlying
1152 NHANES data without model predictions. Note the lack of evidence for any correlation
1153 between iodine intake and fT4 in the NHANES data in the range from 20 to 90 µg/d, in
1154 contrast to model predictions.

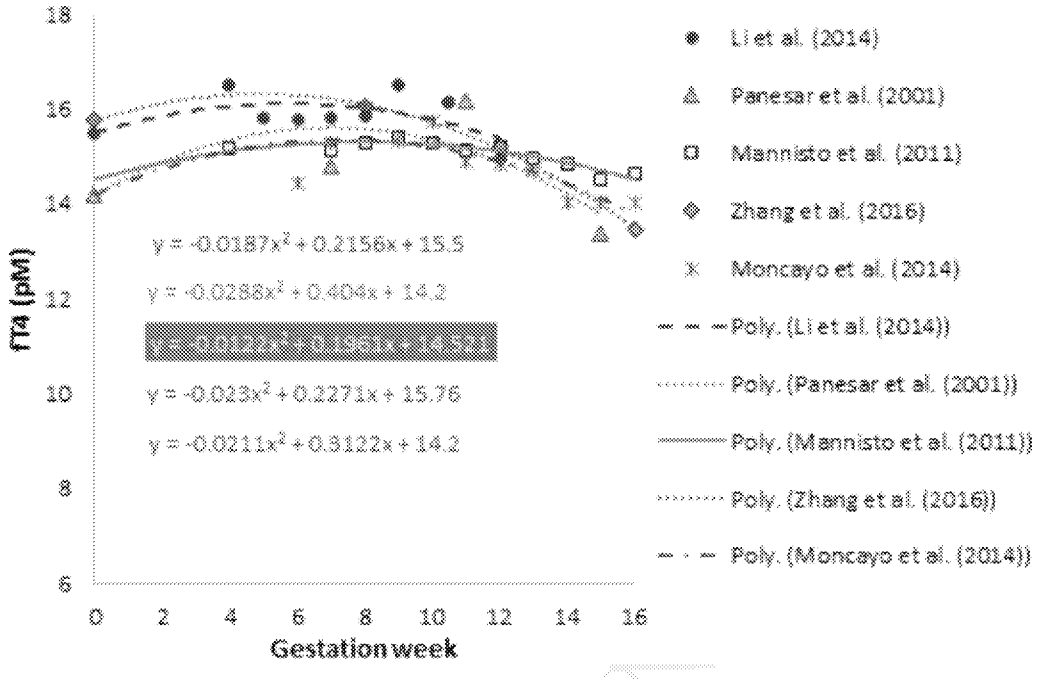
1155 Figure 6. Comparison of BBDR model predicted free T4 (fT4) changes as a function of
1156 perchlorate dose with data from Steinmaus et al. (2016). Reproduced from USEPA (2017).
1157 Blue boxes and diamonds represent the BBDR model predictions for median (170 µg/d) and
1158 low (90 µg/d) iodine intake populations (GW 13-16); red +'s represent the central estimate
1159 from the analysis of the Steinmaus et al. (2016) study and the red x's represent the upper
1160 and lower confidence limits for that estimate.

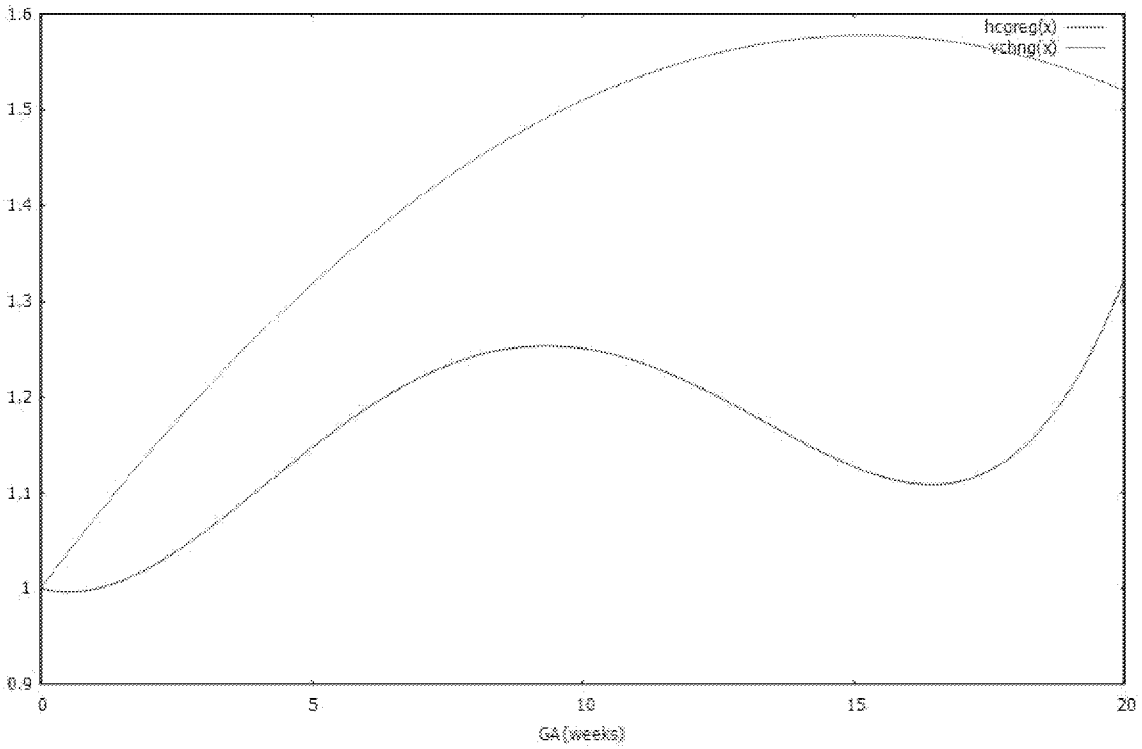
1161 Figure 7. Comparison of PoDs calculated using the USEPA (2017) BBDR model-based PoDs
1162 (blue and green bars) with the USEPA (2005) RfD (red bar).

1163

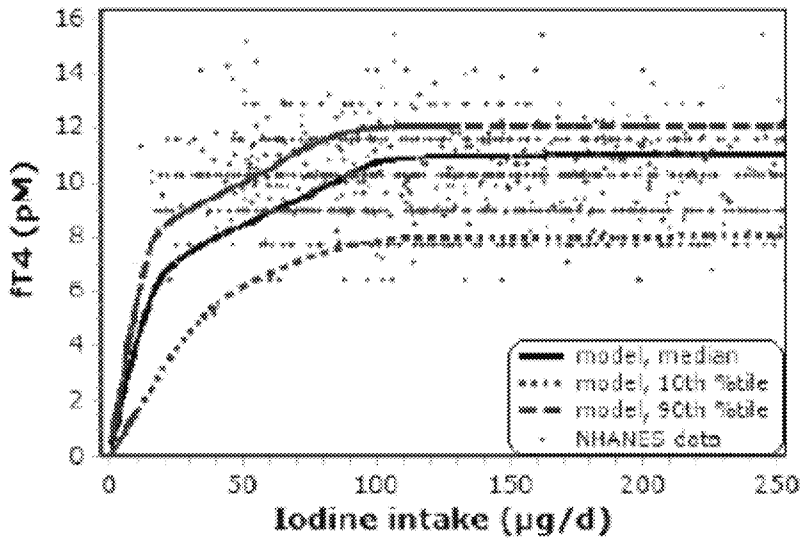








a.



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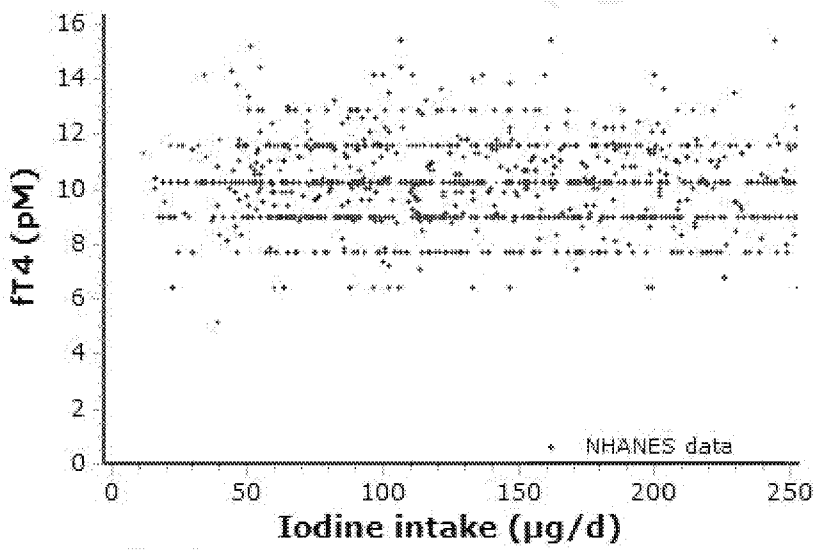

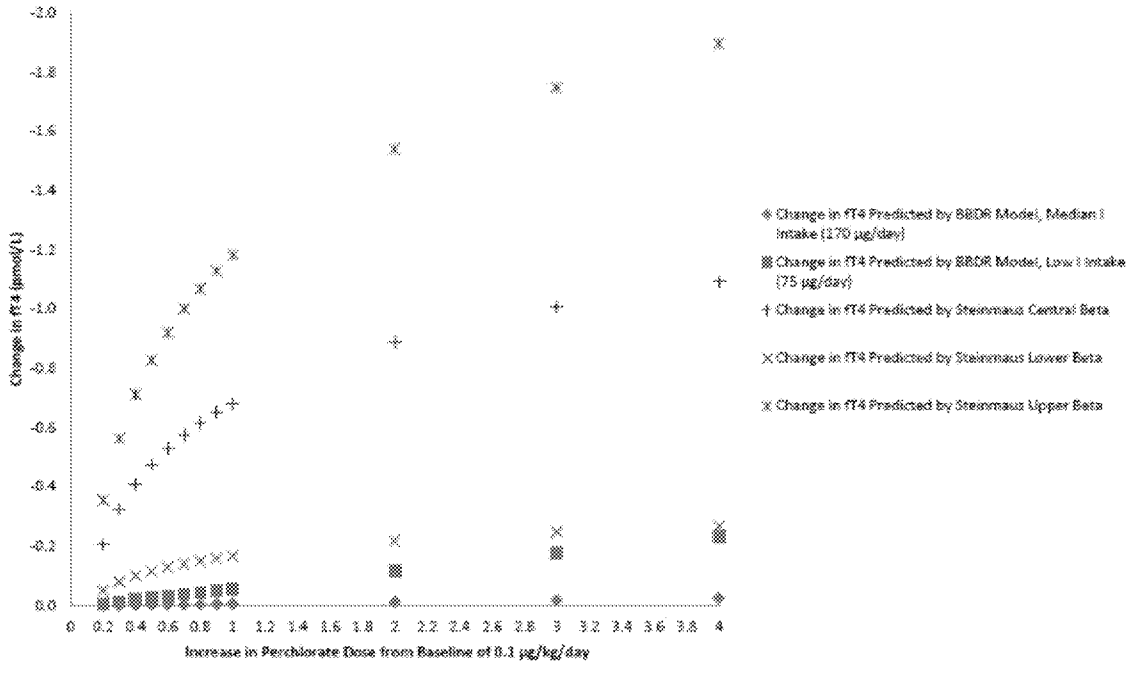

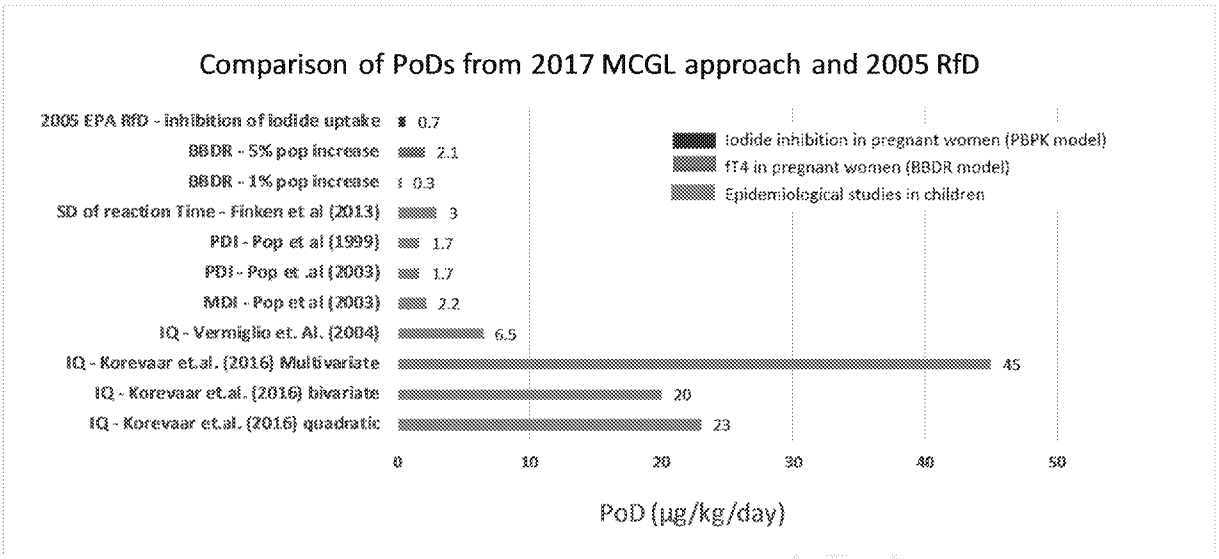

Highlights (maximum 125 characters, including spaces)

- The USEPA (2017) BBDR model plausibly describes perchlorate effects on thyroid hormone regulation during early pregnancy.
- The model is a valuable tool for investigating the effects of perchlorate on thyroid function during early gestation.
- BBDR modeling results indicate that the current USEPA RfD, based on adult effects, is also protective for fetal effects.
- However, current model uncertainties dictate against its use to replace the existing RfD for perchlorate.

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 3/4/2019 7:15:14 PM
To: Mclain, Jennifer [Mclain.Jennifer@epa.gov]; Guilaran, Yu-Ting [Guilaran.Yu-Ting@epa.gov]
CC: Tiago, Joseph [Tiago.Joseph@epa.gov]; Flaharty, Stephanie [Flaharty.Stephanie@epa.gov]; Wadlington, Christina [Wadlington.Christina@epa.gov]; Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: Transmittal Memos for Perchlorate
Attachments: Transmittal Memo EB to JM 3-4-19.docx; Transmittal Memo JM to DR 3-4-19.docx; Transmittal Memo AA to OPEI 3-4-19.docx; Perchlorate Draft Action Memo 3-4-19.docx

Jennifer and Yu-Ting:
Attached for your review and comment are the transmittal memos we are preparing to facilitate Inter Agency Review of the propose perchlorate drinking water standard. We will be preparing the "blue folder"package to facilitate getting these documents to the Office of Policy for transmission to OMB for review. Please note that we have been informed that OGC concurrence requires senior level approval now and we do not expect to receive that concurrence today. Also a reminder that the Action memo is a draft at this stage of the process to identify the information we intend to highlight for the Administrator when it is transmitted for signature after OMB concludes Inter Agency Review.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Newcamp, Caitlin [Newcamp.Caitlin@epa.gov]
Sent: 2/14/2019 8:49:49 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
CC: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: Perchlorate
Attachments: Perchlorate Draft Action Memo 2-14-19.docx

Hi Sam –

Thanks for getting back to me, that sounds good. The attached version is the most recent, but I can send along an updated version as more details arise for the last few sections.

Caitlin

From: Hernandez-Quinones, Samuel
Sent: Thursday, February 14, 2019 2:36 PM
To: Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>
Subject: RE: Perchlorate

Hi Caitlin,

I think you can leave that section as an open item and we can later on decide how that process will be captured in the action memo.

Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Newcamp, Caitlin
Sent: Thursday, February 14, 2019 12:44 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: Perchlorate

Hi Sam, not sure if you're in today,

A couple more questions on perchlorate: was there a workgroup and if so, which offices were/are involved, and was the FAR (final agency review waived)?

Thanks!
Caitlin

From: Hernandez-Quinones, Samuel
Sent: Friday, February 08, 2019 3:52 PM

To: Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>
Subject: RE: Perchlorate

Hi Caitlin

For this document let's assume that the deadline is still April 30, 2019. We have requested an extension till May 30 due to the shutdown, but it has not been granted by the court yet.

Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Newcamp, Caitlin
Sent: Friday, February 08, 2019 3:40 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: Perchlorate

Hey Sam –

Thanks for these. Is there still a deadline of a final rule of Dec 2019 because of the NRDC consent decree? Not clear about the deadlines for the proposed and final rule promulgation.

Caitlin

From: Hernandez-Quinones, Samuel
Sent: Friday, February 08, 2019 10:56 AM
To: Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>
Subject: RE: Perchlorate

Here is the action memo template and the briefing documents I mentioned during our call earlier today.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Newcamp, Caitlin
Sent: Friday, February 08, 2019 10:02 AM

To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: Perchlorate

Hello Sam – You can call me now; going to get coffee with Brynne at 10:30. If it will take longer than 30 minutes I am free after 1. 202-564-0429

From: Hernandez-Quinones, Samuel
Sent: Friday, February 08, 2019 9:58 AM
To: Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>
Subject: Perchlorate

Hi Caitlin,

Let me know when it is a good time to call you today.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 2/4/2019 8:54:44 PM
To: Johnson, Ann [Johnson.Ann@epa.gov]; Dockins, Chris [Dockins.Chris@epa.gov]; Shao, Nicole [Shao.Nicole@epa.gov]; Miller, Gregory [Miller.Gregory@epa.gov]; Flowers, Lynn [Flowers.Lynn@epa.gov]; Foster, Stiven [Foster.Stiven@epa.gov]; Kyprianou, Rose [Kyprianou.Rose@epa.gov]; Miller, Wynne [Miller.Wynne@epa.gov]; Raffaele, Kathleen [raffaele.kathleen@epa.gov]
CC: Christ, Lisa [Christ.Lisa@epa.gov]; Khera, Rajiv [Khera.Rajiv@epa.gov]
Subject: Technical Support Documents - Draft Perchlorate Rule Proposal
Attachments: 181129_DRAFT MCLG TSD.DOCX; Draft Perchlorate HRRCA 2019-02-03.docx; PerchlorateOccMonitoringReport_Updated 2-1-19.docx; Perchlorate T&C November 2018.docx; Perchlorate BAT and SSCT November 2018.docx; WA459_T4_Vol1 Main Report_181113.docx

Preliminary draft for internal EPA review

Hi,

Attached are copies of the draft technical support documents that were used as basis for the Perchlorate Rule Proposal. As mentioned earlier today we are not requesting comments on these documents within the two-week review time frame.

Economic Analysis
MCLG Derivation Document
Treatment Technologies & Costs Document
Occurrence & Monitoring Report
MCLG Approaches Document
Best Available Technologies Document

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Hernandez-Quinones, Samuel
Sent: Monday, February 04, 2019 10:32 AM
To: Cc: Christ, Lisa <christ.lisa@epa.gov>; Burneson, Eric <burneson.eric@epa.gov>; Flaharty, Stephanie <Flaharty.Stephanie@epa.gov>; Messier, Dawn <Messier.Dawn@epa.gov>; Wehling, Carrie <Wehling.Carrie@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: Request for review - Draft Perchlorate Rule Proposal

Preliminary draft for internal EPA review

Hi,

Attached for your review is the Draft Perchlorate Rule Proposal (Preamble and Regulatory Text). As discussed previously we are asking that you provide your questions and or comments on the draft document to me by

COB 2/15/2019. In order to keep with the consent decree deadline, we need to complete this step of the process within two weeks, if there are any issues that require technical discussions please let me know so that we can arrange any necessary working meeting.

I will follow-up with another email later today that contains the draft version of the technical support documents that were used as the basis for the Perchlorate proposal. Since those are very lengthy documents we are not requesting that you submit input and/or comments on those within the two- week time frame.

Please let me know if you have any questions.

Thanks
Sam

==========

Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Lan, Alexis [lan.alexis@epa.gov]
Sent: 7/6/2020 3:52:36 PM
To: Miller, Gregory [Miller.Gregory@epa.gov]
CC: Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]; Albert, Ryan [Albert.Ryan@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Huff, Lisa [Huff.Lisa@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: RE: PFBS assessment
Attachments: SRMD Suggested Edits 7-1-20 DRAFT Interagency and Agency Tox Assessment for PFBS.docx

Hi Greg – please see the revised PFBS comments. Please let us know if there are any questions.

All the best,

Alex Lan, MPH
Physical Scientist
Office of Ground Water and Drinking Water
Standards and Risk Management Division
U.S. Environmental Protection Agency
Washington, D.C.
Lan.Alexis@epa.gov
(Desk) 202.564.0841
(Mobile) 703.303.7791

From: Lan, Alexis <lan.alexis@epa.gov>
Sent: Monday, June 29, 2020 2:33 PM
To: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Cc: Miller, Gregory <Miller.Gregory@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: PFBS assessment

Understood, thank you!

Alex Lan, MPH
Physical Scientist
Office of Ground Water and Drinking Water
Standards and Risk Management Division
U.S. Environmental Protection Agency
Washington, D.C.
Lan.Alexis@epa.gov
(Desk) 202.564.0841
(Mobile) 703.303.7791

From: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Sent: Monday, June 29, 2020 2:27 PM
To: Lan, Alexis <lan.alexis@epa.gov>
Cc: Miller, Gregory <Miller.Gregory@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: PFBS assessment

Hi Alex,

Update….Eric and I meet with Betsy, Greg, and Sam to discuss our comment on the PFBS assessment. First, we heard from Greg that he was successful in getting and extension until 7/8/20 to get OW's comments to ORD. Second, Sam is going to remove much of the comments that provide info re: perchlorate for ORD's consideration. He will send us a revised document.

Take care,
Crystal

From: Lan, Alexis <lan.alexis@epa.gov>
Sent: Wednesday, June 24, 2020 10:54 AM
To: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Subject: RE: PFBS assessment

Thanks Crystal

Alex Lan, MPH
Physical Scientist
Office of Ground Water and Drinking Water
Standards and Risk Management Division
U.S. Environmental Protection Agency
Washington, D.C.
Lan.Alexis@epa.gov
(Desk) 202.564.0841
(Mobile) 703.303.7791

From: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Sent: Wednesday, June 24, 2020 10:48 AM
To: Lan, Alexis <lan.alexis@epa.gov>
Subject: FW: PFBS assessment

For your awareness.

From: Rodgers-Jenkins, Crystal
Sent: Wednesday, June 24, 2020 10:29 AM
To: Behl, Betsy <Behl.Betsy@epa.gov>
Cc: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: RE: PFBS assessment

Betsy, in prep for our meeting with Jennifer and Deborah, see the excerpt below from p. 7 of the Response to Peer Review Comments on the Draft Human Health Toxicity Values for Perfluorobutane Sulfonic Acid (CASRN 375-73-5) and Related Compound Potassium Perfluorobutane Sulfonate (CASRN 29420-49-3)

"Some peer reviewers identified one topic specifically pertaining to uncertainty in interspecies extrapolation (i.e., suggested an increase in UF_A). This reviewer opinion was based on limited human toxicokinetic data in sensitive subpopulations (e.g., pregnancy, children, neonates) and lack of information to quantify relative cross-species sensitivity in thyroid hormone toxicodynamics. The reviewers also provided minor comments primarily regarding textual clarifications in Chapter 6, including:

- Need for additional clarifying language on the physiology and function of thyroid hormones during pregnancy and further description of the clinical condition "hypothyroxinemia";"

This is the point of focus for our conversation with Jennifer.

From: Behl, Betsy <Behl.Betsy@epa.gov>
Sent: Wednesday, June 24, 2020 9:50 AM

To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Nagle, Deborah <Nagle.Deborah@epa.gov>; Erica DiFilippo <ericad@sspa.com>; Tiago, Joseph <Tiago.Joseph@epa.gov>
Subject: RE: PFBS assessment

Jennifer, we would like to have a short meeting to discuss this issue. Erica Weyer will work with Joe Tiago to set the meeting up.

Best, Betsy

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Tuesday, June 02, 2020 2:05 PM
To: Behl, Betsy <Behl.Betsy@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>
Subject: RE: PFBS assessment

Thanks much Betsy. After I sent this note, Eric reminded me that we are primarily working with ORD staff on the perchlorate R2C. So he will make the connection with those folks too.

BTW, what are you thinking about next steps w/FSIS?

From: Behl, Betsy <Behl.Betsy@epa.gov>
Sent: Tuesday, June 2, 2020 1:55 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>
Subject: RE: PFBS assessment

Thanks for the note Jennifer. I will past this on to my staff who are reviewing the ORD document.

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Monday, June 01, 2020 11:31 AM
To: Behl, Betsy <Behl.Betsy@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>
Subject: PFBS assessment

Betsy – you may already be doing this but I wanted to make sure we are connected to ORD as they respond to their peer review comment: Need for additional clarifying language on the physiology and function of thyroid hormones during pregnancy and further description of the clinical condition “hypothyroxinemia”. I’m reviewing the perchlorate response to comment document now and just want to make sure we are being consistent.

Thanks
Jennifer

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 7/1/2020 6:05:17 PM
To: Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]
CC: Christ, Lisa [Christ.Lisa@epa.gov]; Huff, Lisa [Huff.Lisa@epa.gov]
Subject: RE: PFBS assessment
Attachments: SRMD Suggested Edits 7-1-20 DRAFT Interagency and Agency Tox Assessment for PFBS.docx

Hi Crystal,

As discussed during Monday's call I have made revised our input to the PFBS document. Attached is the revised version which incorporates a couple of suggested edits to the PFBS document. Let me know if you have any questions.

Thanks
Sam

==========

Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

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Hi Alex,

Update….Eric and I meet with Betsy, Greg, and Sam to discuss our comment on the PFBS assessment. First, we heard from Greg that he was successful in getting and extension until 7/8/20 to get OW's comments to ORD. Second, Sam is going to remove much of the comments that provide info re: perchlorate for ORD's consideration. He will send us a revised document.

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Subject: RE: PFBS assessment

Thanks Crystal

Alex Lan, MPH
Physical Scientist

Office of Ground Water and Drinking Water
Standards and Risk Management Division
U.S. Environmental Protection Agency
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Lan.Alexis@epa.gov
(Desk) 202.564.0841
(Mobile) 703.303.7791

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This is the point of focus for our conversation with Jennifer.

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Sent: Wednesday, June 24, 2020 9:50 AM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Nagle, Deborah <Nagle.Deborah@epa.gov>; Erica DiFilippo <ericad@sspa.com>; Tiago, Joseph <Tiago.Joseph@epa.gov>
Subject: RE: PFBS assessment

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Best, Betsy

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Subject: RE: PFBS assessment

Thanks much Betsy. After I sent this note, Eric reminded me that we are primarily working with ORD staff on the perchlorate R2C. So he will make the connection with those folks too.

BTW, what are you thinking about next steps w/FSIS?

From: Behl, Betsy <Behl.Betsy@epa.gov>
Sent: Tuesday, June 2, 2020 1:55 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>
Subject: RE: PFBS assessment

Thanks for the note Jennifer. I will past this on to my staff who are reviewing the ORD document.

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Monday, June 01, 2020 11:31 AM
To: Behl, Betsy <Behl.Betsy@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>
Subject: PFBS assessment

Betsy – you may already be doing this but I wanted to make sure we are connected to ORD as they respond to their peer review comment: Need for additional clarifying language on the physiology and function of thyroid hormones during pregnancy and further description of the clinical condition "hypothyroxinemia". I'm reviewing the perchlorate response to comment document now and just want to make sure we are being consistent.

Thanks
Jennifer

Message

From: Strong, Jamie [Strong.Jamie@epa.gov]
Sent: 11/6/2018 1:28:29 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
CC: Behl, Betsy [Behl.Betsy@epa.gov]
Subject: FW: Draft Health Effects Document
Attachments: 181101_INTERIM DRAFT HESD_for EPA.DOCX; 181015_DRAFT HRL Report_2percentIQ gMiller comments 10 22 18 v2.docx

Lisa,
Greg and I talked about perchlorate this morning. When we spoke on the 17th the agreement was that Greg would provide suggestions for clarity or things to cut and any comments on the draft and provide those to you by the 24th. Greg provided those comments (attached) on the 22nd. Greg informed me that he received a new draft title HESD for perchlorate from Sam asking for comment by mid next week. Looking at this draft it's clear that his previous comments were not considered. Were his comments provided to Abt?

Ex. 5 Deliberative Process (DP)

I don't feel like it is a good use of Greg's time to keep reviewing and making the same comments on the document.

I suggest that we reconvene and try to figure out the best way OST can support you all while making the best use of Greg's time.

Jamie

From: Miller, Gregory
Sent: Tuesday, November 06, 2018 7:54 AM
To: Strong, Jamie <Strong.Jamie@epa.gov>
Subject: FW: Draft Health Effects Document

From: Hernandez-Quinones, Samuel
Sent: Friday, November 2, 2018 12:09 PM
To: Miller, Gregory <Miller.Gregory@epa.gov>
Subject: Draft Health Effects Document

Hi Greg,

Here is the draft document that Abt prepared based on our technical direction. Let me know if you have any comments, questions or edits that you want to provide so that the document can be modified as the final version is developed. I will appreciate if you can provide any feedback by mid next week, if possible.

Thank You
Sam
==========

Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 9/27/2018 12:39:27 PM
To: Hanley, Mary [Hanley.Mary@epa.gov]
CC: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: Follow up from perchlorate meeting
Attachments: TO 22 Public Comment Report Final.pdf

Hi Mary,

Here is the 2017 Peer Review (panel #1) public comment summary report.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Hanley, Mary
Sent: Wednesday, September 26, 2018 4:39 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>
Subject: RE: Follow up from perchlorate meeting

Thank you Sam!

From: Hernandez-Quinones, Samuel
Sent: Wednesday, September 26, 2018 4:37 PM
To: Hanley, Mary <Hanley.Mary@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>
Subject: RE: Follow up from perchlorate meeting

The Peer-Review Reports are available under supporting documents in Docket # EPA-HQ-OW-2016-0439. I am Attaching the Reports as well as the public comment summary for the 2018 Peer Review effort.

https://www.regulations.gov/document?D=EPA-HQ-OW-2016-0439-0006

https://www.regulations.gov/document?D=EPA-HQ-OW-2016-0439-0012

I will get the 2017 summary report to you by tomorrow.

Thanks
Sam
==========

Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Burneson, Eric
Sent: Wednesday, September 26, 2018 4:10 PM
To: Hanley, Mary <Hanley.Mary@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: Re: Follow up from perchlorate meeting

Mary
Lease check with Lisa Christ or Sam Hernandez-Quinones who can get you to these documents
Eric
Sent from my iPhone

On Sep 26, 2018, at 3:34 PM, Hanley, Mary <Hanley.Mary@epa.gov> wrote:

> Eric,
> On Nancy's behalf I am trying to find the contractor peer review report for the January 2017 peer review and the contractor's public comment summaries for both the January 2017 and January 2018 contractor peer reviews. I may be missing them but I am not seeing them in either dockets 0438 or 0439. Is there a POC who I can reach out to?
> Thanks
> Mary
> 564-0316
>
> **From:** Burneson, Eric
> **Sent:** Tuesday, September 25, 2018 11:35 AM
> **To:** Beck, Nancy <Beck.Nancy@epa.gov>
> **Cc:** Mclain, Jennifer <Mclain.Jennifer@epa.gov>
> **Subject:** Follow up from perchlorate meeting
>
> Nancy:
> Thanks for your questions at yesterday's briefing on perchlorate, particularly regarding EPA's analysis linking thyroid hormone level changes to IQ decrements. As we discussed, the origin of this analysis was the recommendation of the Science Advisory Board. The SAB stated "The agency should incorporate the appropriate studies related to ingestion of perchlorate, pharmacokinetics of perchlorate, the effects (dynamics) of perchlorate, and dose-response relationships from all the available literature. In developing the pharmacodynamic aspect of this model, the EPA should take advantage of available data on potential adverse health effects due to thyroid hormone perturbations, regardless of the cause of those perturbations, to document and support parameters used in the model. Accordingly, the SAB concludes that these two streams of information — biology of iodide deficiency and perchlorate inhibition of iodide uptake — are complementary and sufficient for the EPA to consider specific life stage factors in deriving an MCLG for perchlorate."
> See https://yosemite.epa.gov/sab/sabproduct.nsf/02ad90b136fc21ef85256eba00436459/d3bb75d4297ca4698525794300522ace!OpenDocument&TableRow=2.3#2 for more information.

Also, you asked about the subsequent peer reviews of the work done to implement the SAB's recommendations. As discussed, we performed these peer reviews in accordance with the Agency's guidance on Contractor Lead Highly Influential Scientific Assessments, which provides the public with opportunities to comment on both the peer reviewers and the draft report. Several of the peer reviewers for the contractor lead peer reviews were also members of the SAB panel. The first peer review focused on the BBDR model's ability to predict thyroid hormone changes associated with perchlorate exposure and the second peer review focused upon the changes made to the BBDR model and the evaluation of epidemiologic studies evaluating the relationship between thyroid changes and neurodevelopmental impacts. We sought input from Federal partners on the peer review charges and they provided comments on the draft reports in the public docket.

The Peer review docket including the peer review reports and the public input can be found at https://www.regulations.gov/docket?D=EPA-HQ-OW-2016-0439.

Also attached for your information is the current version of the scientific analysis that responds to the most recent peer review comments. Please let us know if you have any further questions or concerns that you would like to discuss.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Tucker, Nicole [Tucker.Nicole@epa.gov]
Sent: 9/14/2018 7:54:24 PM
To: Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]
CC: Albert, Ryan [Albert.Ryan@epa.gov]; Wang, Lili [Wang.Lili@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Huff, Lisa [Huff.Lisa@epa.gov]; Carroll, Gregory [Carroll.Gregory@epa.gov]; Hautman, Dan [Hautman.Dan@epa.gov]; Burneson, Eric [Burneson.Eric@epa.gov]; Smith, Lameka [Smith.Lameka@epa.gov]; Koumai, Ouro [Koumai.Ouro@epa.gov]; Goodwin, Kara [goodwin.kara@epa.gov]
Subject: Publication(s) received for review-week of September 10th-September 14th
Attachments: NHEERL Fact Sheet Wang et al. Aug 27 2018(v4).docx; NIS_phase_2_manuscript_v10.docx; SI. Figure S1-3 Tables S2-3.docx; SI. Figure S4. Dose-response for ph2 test chemicals.pdf; SI. Table S1 S4-8 ar.xlsx; OW Advanced notification transmittal NIS Inhibition.docx

Good afternoon Crystal,
OGWDW received one manuscript for review this week. The manuscript reports the results from the screening of ToxCast phase2 chemicals to identify inhibitors of iodide uptake. The study looks at a variety of chemicals including PFAS and uses sodium perchlorate as a reference chemical. I have forwarded the manuscript to TAB and SRRB inquiring interest in reviewing for policy and/or factual error.

Attached is the manuscript and its supplemental documents and below are some details about the review process. Please let me know if you have any questions or concerns. Hope you have a nice weekend!

Sincerely,
Nicole Tucker

Title: High-Throughput Screening and Chemotype-Enrichment Analysis of ToxCast Phase II Chemicals Evaluated for Human Sodium-Iodide Symporter (NIS) Inhibition
Author(s): Jun Wang, Daniel Hallinger, Ashley Murr, Angela Buckalew, Ryan Lougee, Ann Richard, Susan Laws, and Tammy Stoker
Purpose of study: This study reports the results from the screening of ToxCast ph2 chemicals to identify inhibitors of iodide uptake.
Received from: Mary Reiley
OGWDW Reviewer(s): Requested policy reviews from TAB and SRRB; reviewers pending
Review comments requested by: September 27,2018
Comments to be submitted to: OST-Mary Reiley

Nicole Tucker
US Environmental Protection Agency
Office of Ground Water and Drinking Water
Standards and Risk Management Division
202-564-1946

Message

From: Townsend, Clifton [Townsend.Clifton@epa.gov]
Sent: 5/24/2018 9:30:52 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: Need help ASAP!
Attachments: Final_Perchlorate_Response_to_Comments_Document.pdf; Perchlorate_responses to peer review_final_5-13-09.pdf

Oh here it is…I think of RD 2 only…sorry about that.

I have attached the following:

1. Perchlorate responses to comment published in January 2011. I think this what you are looking for. All the other RTC comment docs we had were on the PBPK modeling from 2009.
2. There were the response to the peer review

Clif

From: Christ, Lisa
Sent: Thursday, May 24, 2018 5:01 PM
To: Townsend, Clifton <Townsend.Clifton@epa.gov>
Subject: RE: Need help ASAP!

This is for the 2nd reg det? I don't see perchlorate in there…

From: Townsend, Clifton
Sent: Thursday, May 24, 2018 4:59 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: Need help ASAP!

Sorry for late response.

Clifton

From: Christ, Lisa
Sent: Thursday, May 24, 2018 4:54 PM
To: Townsend, Clifton <Townsend.Clifton@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: Need help ASAP!
Importance: High

Can you please send me the response to comment document from our 2008 preliminary reg det for perchlorate? I want to see what comments we received on the Huber approach to deriving the RSC.
I assume it's in the docket?

Final Comment Response Document for the Regulatory Determination for Perchlorate (Categorized Public Comments)

Office of Water (4607M)
EPA 815-R-10- 005
January 2011
http://water.epa.gov/drink/

Table of Contents

List of Exhibits

1. Introduction and Overview

Background

The U.S. Environmental Protection Agency (EPA or The Agency) is required by the Safe Drinking Water Act (SDWA), as amended in 1996, to publish a list of contaminants (Drinking Water Contaminant Candidate List, or CCL) that are known or anticipated to occur in public water systems, and which may require regulation under the SDWA. The CCL 2 was published in a Federal Register Notice (FR Notice) on February 24, 2005 (70 FR 9071). The Agency is also required to make Regulatory Determinations on at least five of the CCL contaminants following publication. EPA published preliminary regulatory determinations for 11 of 51 total contaminants from CCL 2 on May 1, 2007 (72 FR 24016). In the 2007 notice, perchlorate was not part of the list of 11 contaminants, however, the Agency asked for new information and data related to perchlorate. Subsequently, EPA made a final regulatory determination not to regulate the 11 of the contaminants identified in the May 1, 2007 *Federal Register* notice. Responses to public comment regarding these 11 contaminants were answered as part of the final regulatory determination process and posted to www.regulations.gov (refer to document ID EPA-HQ-OW-2007-0068-0178).

The Agency deferred responding to comments on perchlorate, and issued a separate preliminary determination not to regulate perchlorate on October 17, 2008 (73 FR 66895), followed by an additional public comment period. In a third *Federal Register* notice, issued on August 19, 2009 (74 FR 41883), EPA requested new information and data via public comment. The purpose of issuing the notice was to obtain comments on additional approaches to analyzing data related to EPA's regulatory determination. EPA wanted to ensure consideration of all the potential options for evaluating whether there is a meaningful opportunity for human health risk reduction of perchlorate through a national primary drinking water rule.

This final comment response document presents the comments and responses for all three comment periods. Approximately 39,000 public submissions (in the form of letters, apparent mass mailing campaigns, e-mails, and/or postings to www.regulations.gov) were received by EPA. All original public submissions can be found in their respective docket locations; at www.regulations.gov, under Docket ID EPA–HQ–OW–2007–0068 for the May 2007 notice; EPA–HQ–OW–2008–0692 for the October 2008 notice; and EPA–HQ–OW–2009–0297 for the August 2009 notice.

EPA's Categorization of Public Comments and Document Organization

Within the 3 *Federal Register* notices related to perchlorate, EPA sought public comment on a number of topics, including: regulatory determination; the approach EPA used to make its determination; new data and information; and several other issues specific to the individual FR notices. To address and respond to the public comments that were received, EPA developed a list of numerically ordered topics (referred to as "EPA Comment Codes") that were likely to be addressed by commenters (typically based on the outlines of the draft FR notices). Not all of the EPA Comment Codes were addressed by commenters. The complete list of EPA Comment Codes is provided in Appendix 1, including notation for codes that did not receive comments.

To organize and track public submissions, EPA assigned a document identification (ID) number . These "document IDs" were assigned to give each public submission a unique identifier, and to tie each submission to the docket for the *Federal Register* notice it was submitted under, or to identify it

as the representative letter from an apparent mass mailing campaign (see discussion below regarding mass mailing campaigns).

Each public submission was read by EPA, and, where appropriate, was subdivided into "comment sections," or distinct issue areas, based on topical breaks within the submission. EPA grouped these comment sections (hereinafter referred to as "comments") and assigned a five digit EPA comment identification (ID) number or "comment ID." Comments that were similar in topic were then grouped together into a corresponding EPA Comment Code. Each EPA Comment Code was assigned a four digit reference number.

Apparent Mass Mailing Campaigns – Section 2

EPA received more than 37,000 public submissions from 11 apparent mass mailing campaigns. EPA read each submission and determined if it was part of a campaign. Only one representative letter (the first letter that was received) from each campaign is included in this response to comment document. The representative letters from each campaign appear in their entirety in Section 2 of this report. Each individual letter is presented in the order in which it was originally written, separated into its individual comments (*i.e.*, at topical breaking points), with each comment followed by the associated EPA response (see explanation on the next page regarding cross referencing of responses, and response to comment codes). Each comment from a campaign also appears in Section 3, under its assigned EPA Comment Code.

Comments and Responses by Comment Code – Section 3

Section 3 presents the public comments and EPA's responses. These are organized first by EPA Comment Code, (*i.e.*, the topical subsections within Section 3); then within each Comment Code, comments are organized numerically by EPA Comment ID. Readers can first find the comment code for topics they are interested in, and then find responses to specific Comment IDs for individual comments. The commenter name, organization, and document ID are also given for each comment. Any comment can be read as it appears within the commenter's original letter, e-mail, or posting by searching on the associated Document ID on www.regulations.gov (see explanation of Document IDs in the introduction to this section, "EPA's Categorization of Public Comments and Document Organization"). The Document ID can also be used to find additional information, such as tables or figures, which may be included within the context of comments or attachments in the commenter's original submission.

Cross Referencing of Responses

In many cases, several commenters addressed the same or similar issues. For these comments, EPA has cross referenced responses to avoid redundancy and to ensure consistency. Responses are cross referenced by providing the pertinent EPA Comment ID, along with the EPA Comment Code where the EPA Comment ID is located. As noted above, Section 3 is organized first by EPA Comment Code (the subsections within the chapter), then numerically by EPA Comment ID.

Response to Comment Code

Many comments received by EPA addressed similar topics, and were thus grouped under the same EPA Comment Code. In several of these cases, the same response was appropriate for multiple comments, and EPA developed a "Response to Comment Code" which appears at the beginning of each EPA Comment Code section. Responses to individual comments may point reader to the appropriate Response to Comment Code.

Who Submitted Comments

Because EPA received approximately 39,000 public submissions it is not practical to list all commenters and the topics they commented on. However, in reviewing commenter submissions and profiles, EPA binned commenters into 12 categories to provide a broad characterization of interested stakeholders. Exhibit 1, below, lists commenter category, and the number of comments received within each category.

Exhibit 1: Public Submissions by Category Type

Category Type	Number of Public Submissions
Academia / Professional Societies (including: university departments, professors (even if writing on their own behalf))	10
Consultants	19
Drinking Water Organizations	19
Drinking Water Systems	7
Environmental Groups	44
Federal Government	4
Individual Manufacturers/Companies	2
Industry Groups	14
Local Government	6
States	31
Worker & Public Health Groups	9
Private Citizen and Anonymous Commenters	Approximately 38,817

1. Original documents can be found in the docket at http://www.regulations.gov, under Docket EPA–HQ–OW–2007–0068 for the May 2007 FR; EPA–HQ–OW–2008–0692 for the October 2008 FR; and EPA–HQ–OW–2009–0297 for the August 2009 FR.
2. A complete list of the EPA Comment Codes and their descriptions can be found in Appendix 1.

2. Apparent Mass Mailing Campaigns

Apparent Mass Mailing #1 - Physicians for Social Responsibility

EPA Document ID: EPA-HQ-OW-2008-0692-0081
EPA Comment ID: 19687
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPA's refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692): Perchlorate is a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children. Not regulating this harmful chemical in our drinking water is unacceptable. Perchlorate is found in drinking water in 35 states, and according to the EPA's own data, 16 million Americans are at risk of being exposed to this dangerous chemical.

Response: See response to comment code 6120.

EPA Document ID: EPA-HQ-OW-2008-0692-0081
EPA Comment ID: 19688
EPA Comment Code: 5300

Comment: Setting a standard for perchlorate will absolutely present 'a meaningful opportunity for health risk reduction.' I urge you to do so in accordance with the Safe Drinking Water Act and protect Americans' health.

Response: See response to comment code 5300.

Apparent Mass Mailing #2 - Physicians for Social Responsibility

EPA Document ID: EPA-HQ-OW-2008-0692-0100
EPA Comment ID: 19689
EPA Comment Code: 6120

Comment: The Environmental Protection Agency (EPA), supposedly protecting us against harmful chemicals in our air, water and food, has formally refused to set a drinking- water standard for perchlorate, a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children.

Response: See response to comment code 6120.

EPA Document ID: EPA-HQ-OW-2008-0692-0100
EPA Comment ID: 19690

EPA Comment Code: 5220

Comment: The maximum safe level for perchlorate in drinking water is now 15 times higher than what the EPA declared safe in 2002. Under this new standard, more than 16 million Americans are exposed to unsafe levels of perchlorate in their drinking water, and independent analysis shows anywhere from 20 to 40 million Americans at risk. Perchlorate has been found in the drinking water in 35 states in the U.S.

Response: See response to comment 19873 under comment code 5220.

EPA Document ID: EPA-HQ-OW-2008-0692-0100
EPA Comment ID: 19691
EPA Comment Code: 6120

Comment: The Senate Environment and Public Works Committee has endorsed legislation requiring the EPA to set a federal standard for perchlorate and to monitor levels of the chemical in tap water. Please regulate perchlorate in our drinking water: Your current decision is harmful to public health.

Response: See response to comment code 6120.

Apparent Mass Mailing #3 Group Unidentified

EPA Document ID: EPA-HQ-OW-2008-0692-0561
EPA Comment ID: 19964
EPA Comment Code: 1300

Comment: Docket Identification (ID) Number: EPA-HQ-OW-2008-0692 Preliminary Regulatory Determination on Perchlorate Re: Request for extension of comment period I am writing to express my concern regarding the EPA's failure to regulate perchlorate, as well as the proposed reference level, which fails to protect - and will adversely affect -- the health and development of hundreds of thousands, perhaps millions of American children. EPA has spent a number of years researching perchlorate and developing its conclusions - which are considered highly controversial and complex. They require, therefore, the time for measured and throughful public response. We cannot afford to have this decision rushed through, in the last days of the current administration, and leaving those communities that face the greatest risk without enough time to comment. It takes time for public and community groups to evaluate EPA's findings, review the ever-changing scientific literature, and prepare comments. I therefore request that the EPA extend the 30-day comment period on its October 10, 2008 Preliminary Regulatory Determination on Perchlorate to 90 days.

Response: See the response to comment code 1300. EPA plans to initiate the process of proposing a national primary drinking water regulation for perchlorate (see response to comment code 6120).

Apparent Mass Mailing #4 - Natural Resources Defense Council

EPA Document ID: EPA-HQ-OW-2008-0692-0687
EPA Comment ID: 20016
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460 Dear Administrator Johnson and EPA staff, I urge you to set a drinking water standard for perchlorate that will protect pregnant women and babies nationwide. Perchlorate poses a risk for pregnant women, newborns and young children by interfering with thyroid hormone, which is critical for optimal development of the brain and nervous system. Perchlorate is found in drinking water in at least 26 states, and 20-40 million people could be exposed to this chemical. Several states have set drinking water standards or guidelines for this chemical, but these standards vary widely, so it is critical for the EPA to set a national standard that is based on the best available science and that will protect public health. The EPA's own staff scientists have determined that your decision not to regulate perchlorate places some infants and young children above safe levels of exposure. The EPA's current draft scientific analysis should undergo independent scientific peer review and should be used as the basis for the regulation.

Response:
The Agency believes that further review by the National Research Council would unnecessarily delay regulatory decision making for perchlorate. Therefore, EPA is not, at present, planning to request additional NRC review of issues related to perchlorate. Instead, EPA issued a notice in August of 2009 seeking comments on a broad range of alternative approaches to the interpretation of the scientific data relevant to a regulatory determination for perchlorate in drinking water.

EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

EPA Document ID: EPA-HQ-OW-2008-0692-0687
EPA Comment ID: 20017
EPA Comment Code: 5300

Comment: All Americans deserve healthy and clean drinking water. The EPA should not finalize this decision until the scientific review is complete and should make decisions that are consistent with the agency's own scientists. Contrary to your claims, protecting the health of young children is indeed a "meaningful opportunity for health risk reduction."

Response: See response to comment code 5300.

EPA Document ID: EPA-HQ-OW-2008-0692-0687
EPA Comment ID: 20018
EPA Comment Code: 6120

Comment: Again, I urge you to reverse your decision and to set a national drinking water standard for perchlorate.

Response: See response to comment code 6120.

Apparent Mass Mailing #5 - Clean Water Fund/Clean Water Action

EPA Document ID: EPA-HQ-OW-2008-0692-0689
EPA Comment ID: 20019
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. * perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; * a national primary drinking water regulation would provide a meaningful opportunity to protect public health. Additional Facts * Perchlorate is a harmful chemical used in rocket fuel, flares, and explosives. * Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. * Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills. * EPA agrees that perchlorate has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher.

Response: See response to comment code 6120.

Apparent Mass Mailing #6 - Earth Justice

EPA Document ID: EPA-HQ-OW-2008-0692-0972
EPA Comment ID: 20884
EPA Comment Code: 6120

Comment: Administrator Stephen L. Johnson 1101A EPA Headquarters 1200 Pennsylvania Avenue, NW, Ariel Rios Building Washington, DC 20460 Subject: Protect Our Drinking Water From Perchlorate Contamination Dear Administrator Johnson, I am writing to urge you reverse EPA's preliminary regulatory determination and set a protective drinking water standard for perchlorate as required by the Safe Drinking Water Act. Perchlorate contamination in our food and water supplies is too widespread, and its toxic effects too well known, for continued inaction on this problem.

Response: See response to comment code 6120.

EPA Document ID: EPA-HQ-OW-2008-0692-0972
EPA Comment ID: 20885
EPA Comment Code: 5240

Comment: Many experts disagree with your assessment that drinking water with 15 parts per billion of perchlorate is safe and acceptable. Scientists from the California Environmental Protection

Agency and the Massachusetts Department of Environmental Protection have set stricter standards to will ensure that the most vulnerable populations -- pregnant women, infants, and small children -- are protected from the adverse impacts of perchlorate.

Response: See response to comment code 5220.

EPA Document ID: EPA-HQ-OW-2008-0692-0972
EPA Comment ID: 20886
EPA Comment Code: 4000

Comment: EPA's analysis fails to consider that the combination of food and drinking water exposure to perchlorate in the U.S. population exceeds the reference dose set by EPA. Nor does it incorporate the more protective methodology behind the recent state regulatory actions. These flaws must be remedied for the sake of the millions of U.S. families exposed to dangerous levels of perchlorate contamination.

Response: EPA considers the combination of food and drinking water through the relative source contribution (RSC). The RSC is the percentage of the reference dose remaining for drinking water after other sources of exposure to perchlorate have been considered (e.g., food). See the August 2009 Federal Register notice (41887) for a detailed discussion of RSC derivation.

Regarding the comment about incorporating methodologies behind recent state regulatory actions, States use different methodologies or assumptions to derive their own standard based on their unique exposure scenarios. EPA has used the best available peer reviewed science in making this regulatory determination.

Apparent Mass Mailing #7 – Group Unidentified

EPA Document ID: EPA-HQ-OW-2008-0692-1518
EPA Comment ID: 20705
EPA Comment Code: 6120

Comment: I understand the dangers of perchlorate and ask you to keep the testing requirement intact for our public drinking water supplies. Removal of the testing requirement would eliminate detection of perchlorate in the case of accidental or intentional contamination of drinking water supplies, such as the Tewksbury Massachusetts contamination in 2004.

Response: See response to comment code 6120.

Apparent Mass Mailing #8 - Food and Water Watch

EPA Document ID: EPA-HQ-OW-2008-0692-1805
EPA Comment ID: 20883

EPA Comment Code: 6120

Comment: Dear Administrator Johnson, I am writing to urge you to reconsider EPA's preliminary determination not to regulate perchlorate in drinking water. Perchlorate has been found in the drinking water supply of 35 states and the District of Columbia. Widespread human exposure to perchlorate was confirmed by the Center for Disease Control's NHANES study, which found that 100 percent of the 2,820 randomly selected study participants had detectable levels of perchlorate in their urine. The widespread exposure of the population to some level of perchlorate raises serious health concerns. Perchlorate can inhibit the thyroid gland's iodine uptake, potentially leading to hypothyroidism. Severe hypothyroidism during pregnancy can lead to abnormal fetal cognitive development, and even mild hypothyroidism during pregnancy is associated with subtle cognitive defects in children. Thus, perchlorate could alter fetal brain development, having lifelong cognitive effects for those affected. EPA's failure to regulate perchlorate in drinking water places consumers - especially children and pregnant women - at risk. In response to this misguided determination, EPA's own Children's Health Protection Advisory Committee has drafted a letter expressing its concern with EPA's decision not to regulate perchlorate. Members of the committee claim that EPA rushed a decision on perchlorate without taking time to consider all the latest peer-reviewed studies. Given the vital importance of fetal central nervous development not only for long-term health and development of children, but also for the viability of fetuses, why would EPA rush to a decision? Unfortunately, the only conclusion we can draw is that EPA has issued this determination to avoid strapping the Department of Defense with costs to clean up near military bases, missile testing sites and chemical plants. While millions of consumers' health is jeopardized, it seems the budget concerns of the Pentagon or White House are driving EPA's decision. This determination is clearly another instance of a regulatory agency shirking its responsibility to protect the American public. Instead of fulfilling its obligations under the SDWA, EPA has once again folded to pressure.

Response: See response to comment code 6120.

Apparent Mass Mailing #9 - Group Unidentified

EPA Document ID: EPA-HQ-OW-2008-0692-2366
EPA Comment ID: 29116
EPA Comment Code: 6120

Comment: Water Docket, EPA, Mailcode 2822T 1200 Pennsylvania Ave., NW Washington, DC 20460 To Whom It May Concern: I urge you to reverse your decision and set a federal limit for perchlorate in drinking water. Perchlorate is a nationwide problem and has health impacts at lower levels than previously thought. Please protect public health, especially infants and children, by regulating perchlorate.

Response: Please see the response to comment code 6120.

Apparent Mass Mailing #10 - Group Unidentified

EPA Document ID: EPA–HQ–OW–2009–0297-0039
EPA Comment ID: 28365
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate. perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; protecting infants and children is critical. a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Response: See response to comment code 6120.

Apparent Mass Mailing #11 - Food and Water Watch

EPA Document ID: EPA–HQ–OW–2009–0297-0526
EPA Comment ID: 28614
EPA Comment Code: 6120

Comment: Administrator Jackson USEPA Headquarters Ariel Rios Building 1200 Pennsylvania Avenue, N. W. Washington, DC 20460 September 18, 2009 Dear Administrator Jackson, I am writing, on behalf of Food and Water Watch, to urge you to make a national primary drinking water rule for perchlorate. Perchlorate has been found in the drinking water supply of 35 states and the District of Columbia. Widespread human exposure to perchlorate was confirmed by the Center for Disease Control's NHANES study, which found that 100 percent of the 2,820 randomly selected study participants had detectable levels of perchlorate in their urine. And according to your request for comment notice, dated August 5, 2009, the number of people served by water contaminated with high levels of perchlorate ranges between 53.4 and 16.8 million people.

Response: See response to comment code 6120.

EPA Document ID: EPA–HQ–OW–2009–0297-0526
EPA Comment ID: 28615
EPA Comment Code: 2150

Comment: Your decision to not request additional NRC review of issues relating to perchlorate is ill advised. Additional NRC research may better elucidate the health effect and exposure risk we presently face. Moreover, NRC research may provide better guidance in making a final regulatory determination, especially in determining the best health reference level (HRL).

Response: Please see the response to comment ID 28822 under comment code 2150.

EPA Document ID: EPA–HQ–OW–2009–0297-0526
EPA Comment ID: 28616
EPA Comment Code: 5225

Comment: As suggested by previous commenter's, I believe that the Agency's proposed HRL, of 15 micrograms/Liter, is too high. The alternative HRLs presented in Table 2 of your request for comment notice, dated August 5, 2009, do not use the most appropriate data. The data in Table 2 uses mean ingestion rates from the CSFII. The CSFII is already several years out of date.

Response: Regarding the Agency's proposed HRL of 15 ug/L being too high, see response to comment code 5220. Regarding use of CSFII data, EPA believes that it is the best peer reviewed science that is available.

EPA Document ID: EPA–HQ–OW–2009–0297-0526
EPA Comment ID: 28617
EPA Comment Code: 3170

Comment: You also request comment on how the Agency should account for variation of perchlorate levels over time in public water systems. This is simple: the Agency should act with extreme precaution.

Response: See response to comment code 6120.

EPA Document ID: EPA–HQ–OW–2009–0297-0526
EPA Comment ID: 28618
EPA Comment Code: 6120

Comment: The widespread exposure of the population to some level of perchlorate raises serious health concerns. Perchlorate can inhibit the thyroid glands iodine uptake, potentially leading to hypothyroidism. Severe hypothyroidism during pregnancy can lead to abnormal fetal cognitive development, and even mild hypothyroidism during pregnancy is associated with subtle cognitive defects in children. Thus, perchlorate could alter fetal brain development, having lifelong cognitive effects for those affected. EPA's failure to regulate perchlorate in drinking water places consumers, especially children and pregnant women, at risk. We urge the EPA to consider the regulation of perchlorate as an opportunity to protect our waterways and make our drinking water safe for all.

Response: See response to comment code 6120.

3. Comments and EPA Responses by Comment Code

EPA Comment Code: 1000 General Comments

Individual Comments

Commenter Name: Julie L. Heckman
Commenter Organization: American Pyrotechnics Association (APA)
EPA Document ID: EPA-HQ-OW-2009-0297-0522
EPA Comment ID: 28489
EPA Comment Code: 1000

Comment: Please see the attached comments of the American Pyrotechnics Association.

Attachment

September 18, 2009

EPA Docket Center (Water Docket) U.S. Environmental Protection Agency EPA West Building 1301 Constitution Ave., N.W., Room: 3334, Mail Code: 2822T Washington, DC 20004

Re: Drinking Water: Perchlorate Supplemental Request for Comments, 74 Fed. Reg. 41883 (Aug. 19, 2009); Docket ID No. EPA-HQ-OW-2007-0297; RIN 2040-AF08

Dear Sir or Madam:

These comments are submitted on behalf of the American Pyrotechnics Association ("APA"), in response to the above-referenced Notice and Supplemental Request for Comments ("Notice") appearing in the Federal Register on Wednesday, August 19, 2009. We appreciate the opportunity to provide the Agency with these comments.

Interest of the APA

The APA is the principal safety and trade association of the fireworks industry representing manufacturers, importers, distributors, retailers, suppliers, and professional public display firms. The APA has over 240 member companies. Along with their subsidiaries, APA member companies are responsible for 90 percent of the fireworks manufactured, imported, distributed and displayed in the U.S.

The fireworks industry is predominately comprised of small family businesses that together, on one day each year, serve almost all of the nation and its citizens with the very special honor of celebrating this country's most patriotic of holidays, Independence Day, the Fourth of July. This is a responsibility entrusted to us by the founders themselves.

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Julie L. Heckman
Commenter Organization: American Pyrotechnics Association (APA)
EPA Document ID: EPA-HQ-OW-2009-0297-0522
EPA Comment ID: 28491
EPA Comment Code: 1000

Comment: Perchlorate has recently been used in fireworks because it is essential to the formula to cause the fireworks compositions to burn properly. The perchlorate formulas replaced chlorate formulas, which were less stable and highly friction sensitive, in order to provide a much safer product. The perchlorate formulas are designed so that the perchlorate is consumed during combustion. Efforts to replace perchlorate continue, but the technology for a safe, equally effective substitute is still developing.

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0649
EPA Comment ID: 28494
EPA Comment Code: 1000

Comment: October 7, 2009

U.S. Environmental Protection Agency Mailcode 2822T 1200 Pennsylvania Ave., NW. Washington, DC 20460

Subject: Docket ID No. EPA-HQ-OW-0297

Reference: Drinking Water: Perchlorate Supplemental Request for Comments (Federal Register / Vol. 74, No. 159 / Wednesday, August 19, 2009 / Notices

This letter is submitted to correct and clarify comments provided by the Nevada Division of Environmental Protection (NDEP) dated September 16, 2009 in response to the referenced "Supplemental Request for Comments" noticed by the U.S. Environmental Protection Agency (EPA) in the August 19, 2009 Federal Register; Docket ID No. EPA-HQ-OW-2009-0297.

The modifications to our earlier submittal concern the description of analytical methods and detection limits associated with perchlorate data collected and reported by the Metropolitan Water District (MWD) of Southern California for the Whitsett Intake. The NDEP is providing these corrections even though these corrections do not change the NDEP's analyses or recommendations provided in our original submittal.

The necessary corrections relate to several dates and a reporting limit that were provided on page 16 of 22 within the referenced submittal. Specifically, following submittal of initial comments by the NDEP, it came to our attention that:

* A change from a reporting limit of 4 ug/L to 2 ug/L occurred early than was referenced; * A change from EPA Method 314 to EPA Method 331 occurred earlier than was referenced; * A change from EPA Method 331 to EPA Method 332 occurred earlier than was referenced; and * The MWD is being provided a 0.1 ug/L reporting limit for EPA Method 331 and EPA Method 332.

A corrected page 16 of 22 to the September 16, 2009 NDEP submittal is attached to this letter to serve as an errata replacement page to our earlier submittal. Track change mode was used to provided clarity and transparency related to this revision. Please use the provided errata to update your records. Additionally, please contact the undersigned should you wish to discuss these data further.

The NDEP appreciates this opportunity to provide the EPA with helpful information to enable the EPA to make a thoughtful and credible decision regarding whether there is a meaningful opportunity for health risk reduction to persons served by public water systems through promulgating a national drinking water rule for perchlorate.

Sincerely, Tom Porta, Deputy Administrator Nevada Division of Environmental Protection

Tp/tjc cc Jennifer Carr, P.E., CEM, Chief, Bureau of Safe Drinking Water, Nevada Division of Environmental Protection, 901 S. Stewart Street, Suite 4001, Carson City, NV 89701-5249 Darrel Osterhoudt, Regulatory Affairs Manager, Association of State Drinking Water Administrators, 1401 Wilson Blvd., Suite 1225, Arlington, VA 22209 Kay Brothers, Deputy General Manager, SNWA Engineering/Ops, Southern Nevada Water Authority, 100 City Parkway, Suite 700, Las Vegas, NV 89106 Dr. Mic Stewart, Manager, Water Quality Section, Metropolitan Water District of Southern California, 700 North Alameda Street, Los Angeles, CA 90012 Marie Pearthree, Assistant General Manager, Central Arizona Water Conservation District, PO Box 43020, Phoenix, AZ 85080-3020 Brenda Pohlmann, Environmental Programs Manager, City of Henderson, PO Box 95050, Henderson, NV 89009 Susan Crowley, Tronox, LLC, PO Box 55, Henderson, NV 89009 Jeff Gibson, AMPAC, 3883Howard Hughes Parkway, Suite 70, Las Vegas, Nevada 89109

Attachment [See PDF docket ID EPA-HQ-OW-2009-0297-0649; this corrects docket ID EPA-HQ-OW-2009-0297-0638]

Response: No response is necessary to the information provided by the commenter and the errata sheet.

Commenter Name: Anthony Russo
Commenter Organization: Chemistry Council of New Jersey (CCNJ)
EPA Document ID: EPA-HQ-OW-2009-0297-0673
EPA Comment ID: 28691
EPA Comment Code: 1000

Comment: An arbitrarily low standard for perchlorate could result in misdirected regulatory action against any and all low level contaminants in our water supply and the negative public health impacts that will follow from that.

CCNJ appreciates this opportunity to comment. We believe that the scientific evaluation of perchlorate has become quite complicated over the past few years and that there is still the need for study and debate. We hope that CPA will carefully consider our comments.

Sincerely, Anthony Russo Director of Regulatory Affairs CCNJ

Response: Please see the response to comment code 6120.

Commenter Name: Janice Dunn
Commenter Organization: California Space Authority (CSA)
EPA Document ID: EPA-HQ-OW-2009-0297-0671
EPA Comment ID: 28692
EPA Comment Code: 1000

Comment: October 6, 2009

Ms. Lisa P, Jackson Administrator U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, NW Washington, DC 20460

RE: EPA-HQ-OW-2009-0297, "Drinking Water: Perchlorate - Supplemental Request for Comments," 74 FR 159:41883, 19 August 2009

Dear Ms. Jackson:

The California Space Authority (CSA) is a nonprofit corporation representing the commercial, civil, and national defense/homeland security interests of California's diverse space enterprise community. Therefore, we feel compelled to share our concern regarding the Environmental Protection Agency (EPA) request for public comments regarding data related to EPA's perchlorate regulatory determination (the Notice; U.S. EPA, 2009b).

Earlier this year, President Obama issued a broad directive that would guarantee scientific integrity in all federal policy making. We strongly support this policy standard. CSA believes that additional approaches proposed by EPA which support a possible regulatory determination are consistent with this directive.

There is a substantial body of scientific evidence related to the health risks associated with perchlorate. Five decades of scientific investigation, including a landmark National Academy of Sciences (NAS) review, result in a clear and consistent conclusion: low levels of perchlorate are not dangerous to public health.

CSA respectfully requests that the EPA support sound public policy which protects human health and is based on solid science standards.

Sincerely, Janice Dunn Deputy Director

Response: Please see the response to comment code 6120.

Commenter Name: Robert E. Brackett

Commenter Organization: Grocery Manufacturers Association (GMA)
EPA Document ID: EPA-HQ-OW-2009-0297-0413
EPA Comment ID: 28705
EPA Comment Code: 1000

Comment: GMA appreciates the opportunity to provide comments on the public notice regarding alternative approaches to the interpretation of the scientific data relevant to a regulatory determination for perchlorate in drinking water.

Attachment

September 18, 2009

Water Docket Environmental Protection Agency Mailcode 2822T 1200 Pennsylvania Avenue, NW Washington, DC 20460

RE: Docket No. EPA-HQ-OW-2009-0297, "Drinking Water: Perchlorate - Supplemental Request for Comments," 74 FR 159:41883, 19 August 2009

Dear Sir/Madam:

The Grocery Manufacturers Association (GMA) represents the world's leading food, beverage and consumer products companies. The Association promotes sound public policy, champions initiatives that increase productivity and growth and helps to protect the safety and security of the food supply through scientific excellence. The GMA board of directors is comprised of chief executive officers from the Association's member companies. The $2.1 trillion food, beverage and consumer packaged goods industry employs 14 million workers, and contributes over $1 trillion in added value to the nation's economy.

GMA appreciates this opportunity to provide comments on the above referenced public notice regarding alternative approaches to the interpretation of the scientific data relevant to a regulatory determination for perchlorate in drinking water.

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28826
EPA Comment Code: 1000

Comment: AMWA's comments are presented in two parts. The first part focuses on several areas where AMWA requests clarification or makes recommendations including: EPA's alternative HRL analysis, review of this analysis and the PBPK model by the National Academies National Research Council, EPA's population estimates, the Inspector General (IG) report, the significance of the reference dose (RfD) being set at a no observed effect level (NOEL) rather than a no observed adverse effect level (NOAEL), and the science surrounding perchlorate. The second part of the

letter provides responses to three issues where EPA specifically requested comment in the Federal Register (FR) notice.

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 29080
EPA Comment Code: 1000

Comment: Is perchlorate known to occur or is there a substantial likelihood that perchlorate occurs at a frequency and at a level of public health concern in public water systems?

Perchlorate is not known or likely to occur in public water systems with high enough frequency nor does it occur at levels of public health concern. The NHANES studies and breast milk biomonitoring studies, notwithstanding their limitations, reveal that the US population is not exposed to levels of perchlorate that could cause an adverse effect, even when all exposure sources - in food and water - are considered.

In the NHANES results, Americans 6 years and older had a 50th percentile dose of perchlorate at the time of sampling equivalent to 2.2 ppb in drinking water. (Blount, 2006) This dose is less than 10 percent of the conservative NOEL level that is the basis of EPA's RfD and 7,000 times lower than the NOAEL. Less than 0.004% of the population has the potential for exposure to perchlorate above the RfD. (Blount, 2006) By all standard regulatory benchmarks EPA uses to determine acceptable incremental potential population risk from drinking water exposure, total perchlorate exposure has not required regulation. If total exposure does not present a meaningful risk for regulatory purposes, it follows that the risk from exposure to perchlorate in drinking water only is even smaller.

The sole effect of setting a drinking water standard would be to reduce this already insignificant fraction. Rarely does EPA have both toxicology and exposure measures of such high quality. This evidence shows that drinking water is not a significant source of perchlorate for the population.

The nationally-representative Unregulated Contaminant Monitoring Rule 1 results show that perchlorate does not occur frequently or at levels of public health concern in public water systems. The process for collecting data on unregulated contaminants in large and small water systems has been well established and relied upon by EPA for past Contaminant Candidate List (CCL) regulatory determinations. The UCMR is the most complete source of information on contaminant occurrence in the nation's drinking water sources. The use of UCMR sampling data for regulatory determinations has been well established.

Response: EPA has determined that perchlorate occurs or there is a substantial likelihood that perchlorate will occur with a frequency and at levels of health concern in public water systems. Therefore, EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

EPA disagrees with the interpretation of the NHANES studies and breast milk monitoring revealing that the US population is not exposed to levels of perchlorate that could cause an adverse effect. The NHANES studies did not measure exposure in infants and children under the age of 6. In light of the discussion presented in the final regulatory determination notice and the information available at this time, EPA believes that a NPDWR for perchlorate could reduce perchlorate exposures to levels below the potential alternative HRLs.

EPA disagrees with the statement that the UCMR 1 results show that perchlorate does not occur frequently or at levels of public health concern in public water systems. EPA believes that the UCMR 1 is the best available data on the frequency and level of perchlorate occurrence in public water systems nationally. UCMR 1 indicated that 5.1 to 16.6 million people are served by PWSs, for which we have data, that have detected perchlorate at levels above the potential health levels.

EPA Comment Code: 1100 SDWA requirements and the CCL and Regulatory Determinations process

Individual Comments

Commenter Name: James Taft
Commenter Organization: Association of State Drinking Water Administrators (ASDWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0169
EPA Comment ID: 20285
EPA Comment Code: 1100

Comment: States are also very interested in the contaminants for which a decision has not yet been proposed but where EPA shared information in the notice on the status of its analysis of these chemicals. Contaminants in this category include MTBE and perchlorate. ASDWA appreciates the fact that EPA chose to share extensive information on these contaminants in the notice, since some of these contaminants are "hot" topics in many states. Even if regulatory decisions are not yet made, states need to know the current status to help them deal with public water systems where these contaminants have been found. ASDWA encourages EPA to continue to provide information on the status of their regulatory deliberations especially for contaminants like MTBE and perchlorate where there has been significant public and legislative interest. ASDWA and individual states are ready to assist and provide input to EPA's decision making at any time. We offer the following specific observations about perchlorate, metolachlor, and MTBE .

Response: See response to comment ID 20264 under comment code 7100.

Commenter Name: James Taft
Commenter Organization: Association of State Drinking Water Administrators (ASDWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0169
EPA Comment ID: 20287
EPA Comment Code: 1100

Comment: National regulations covering a contaminant that may be a very localized problem need to be considered very carefully. They must be supported by scientific data. If further information is needed on the sources of human exposure, states urge the Agency to consider such additional documentation before a regulatory determination is made. If analysis of additional data does support regulation, states do not believe there is adequate justification for establishing a new national drinking water standard. Under such circumstances, its primary impact would be to add more water quality monitoring without necessarily enhancing public health protection. If an MCL is eventually developed based on somewhat localized occurrence patterns, we would encourage the Agency to consider requiring targeted monitoring, based on preliminary initial rounds of monitoring, rather than uniform monitoring across the board.

Response: EPA intends to develop monitoring requirements for perchlorate as part of a proposed National Primary Drinking Water Regulation.

Commenter Name: D. Daley

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1625
EPA Comment ID: 20564
EPA Comment Code: 1100

Comment: Please include perchlorate on the EPA's Contaminant Candidate List. I am concerned with the potential health risks to all living things from exposure to perchlorate, especially in drinking water. By leaving this contaminant on the EPA's Contaminant Candidate List, it will be given attention needed to control it's use and disposal properly and safely to prevent significant future pollution problems to the environment. As a licensed professional engineer with the State of Connecticut, I urge you to reverse the EPA's decision to remove this dangerous contaminant from the CCL and place it back on the CCL as it should be there. Please help keep this dangerous chemical out of our drinking water.

Response: EPA included perchlorate on the first, second, and third Contaminant Candidate Lists that were published in the Federal Register on March 2, 1998 (63 FR 10273), February 24, 2005 (70 FR 9071), and October 8, 2009 (74 FR 51850), respectively. EPA has decided to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Ron Curry
Commenter Organization: New Mexico Environment Department
EPA Document ID: EPA-HQ-OW-2008-0692-1796
EPA Comment ID: 20940
EPA Comment Code: 1100

Comment: Furthermore, section 1412(b)(3)(A) of the SDWA requires that the EPA Administrator, when making a decision based on science, shall use "the best available peer-reviewed science and supporting studies conducted in accordance with sound and objective scientific practices."[FN27: 42 U.S.C. [section] 300g-1(b)(3)(A) (Westlaw 2008).] However, according to EPA's Science Advisory Board (SAB), EPA's preliminary determination not to regulate perchlorate "relies on the use of a dosimetric model which is now undergoing letter peer review."[FN28: Letter from Dr. Deborah L. Swackhammer, Chair, EPA Science Advisory Board, and Dr. Joan Rose, Chair, EPA Science Advisory Board, Drinking Water Committee, to EPA Administrator Stephen L. Johnson, at 1 (Nov. 5,2008).] Yet EPA plans to make a final determination whether to regulate perchlorate by December 2008.[FN29: 73 Fed. Reg. at 60281.] Consequently, the SAB has expressed concern that the soundness of the dosimetric model "will not be publicly vetted."[FN30: Letter from Dr. Swackhammer & Dr. Rose, at 1.] The SAB stresses the importance of such peer review: "The quality of the scientific foundation for EPA's decisions depends on peer review, which brings a variety of scientific perspectives to bear on critical components of EPA's decisions. Where science assessments have been conducted with the benefit of external scrutiny, the end products have been better able to support the policy making process."[FN31: Id. at 2.7] It is critical, therefore, that EPA make the determination whether to regulate perchlorate with the benefit of fully peer-reviewed, and publicly- scrutinized scientific analysis. Failure of EPA to do so would be arbitrary and capricious and not in accordance with the requirements of the SDWA.

Thank you for your consideration of these comments.

Ron Curry Cabinet Secretary

cc:Governor Bill Richardson Sarah Cottrell, Office of the Governor Attorney General Gary King Stephen R. Farris, Office of the Attorney General

Response: Administrator Stephen Johnson replied to the SAB on January 9, 2009. The letter is available in EPA's docket ID No. EPA-HQ-OW-2009-0297 for this notice. EPA agrees with the commenter that it is critical that EPA make the determination whether to regulate perchlorate with the benefit of fully peer-reviewed scientific analysis, which is available to the public. This comment was received prior to EPA's peer-review process for the PBPK (dosimetric) model, which has now been completed. EPA has made this determination based on a consideration of the best available peer reviewed science and data collected in accordance with accepted methods related to perchlorate occurrence in drinking water, the presence of perchlorate in foods, and the potential health effects of exposure to perchlorate.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20983
EPA Comment Code: 1100

Comment: BACKGROUND

In 1974, Congress enacted the federal Safe Drinking Water Act (SDWA) to protect the public health from contaminated drinking water supplies by regulating public drinking water systems. The SDWA was amended in 1986 and 1994, and requires EPA, inter alia, to publish national primary drinking water regulations, which must include both non-enforceable, health-based Maximum Contaminant Level Goals (MCLGs) and enforceable Maximum Contaminant Levels (MCLs).[FN7: 42 U.S.C. §300g-1(a)(1).] The MCLG must be set "at the level at which no known or anticipated adverse effects on the health of persons occur and which allows for an adequate margin of safety."[FN8: 42 U.S.C. §300g-1(b)(4)(A).] In contrast, the MCL, the maximum level of a regulated contaminant that any particular covered public water system may deliver to any user, must be set "as close to the maximum contaminant level goal as is feasible."[FN9: 42 U.S.C. §300g-1(b)(4) (B).] SDWA requires EPA to set a national primary drinking water standard when it determines for a contaminant that:

(i) the contaminant may have an adverse effect on the health of persons; (ii) the contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and (iii) in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.[FN10: 42 U.S.C. §300g-1(b) (1)(A).]

SDWA also requires EPA to establish a "contaminant candidate list" (CCL) identifying a list of contaminants, not yet regulated by the Agency, which are known or anticipated to occur in drinking water and which may require regulation.[FN11: 42 U.S.C. §300g-1(b)(1)(B).] Every five years, EPA must determine whether or not to regulate five of the contaminants that appear on the CCL.[FN12: Id.] In March, 1998, EPA's first CCL included perchlorate, but the Agency did not choose to make any determination about whether to regulate the contaminant. In February, 2005, EPA announced

its second CCL, CCL2, on which perchlorate appeared again. As a result of its status as a candidate contaminant, EPA subsequently announced this preliminary determination on perchlorate.

Response: No response necessary to the information provided by the commenter.

Commenter Name: Gregg Grunenfelder
Commenter Organization: National Drinking Water Advisory Council (NDWAC)
EPA Document ID: EPA-HQ-OW-2008-0692-2010
EPA Comment ID: 21008
EPA Comment Code: 1100

Comment: November 26, 2008

Mr. Stephen L. Johnson Administrator U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W. Washington D.C. 20460

Dear Administrator Johnson:

In follow-up to EPA's October 10, 2008 preliminary regulatory determination for perchlorate in drinking water, the National Drinking Water Advisory Council (NDWAC) would like to again convey to EPA the necessity for more thorough health effects research to support Safe Drinking Water Act (SDWA) related regulations. While NDWAC members do not have a consensus position to relay on the perchlorate decision itself, the members fully support the need for a strong, scientifically valid basis upon which to make such decisions.

On June 24, 2008, the NDWAC expressed to you our recommendation for a holistic drinking water research plan that includes the needed health effects research for Contaminant Candidate List (CCL) contaminants. The NDWAC strongly supports the CCL process and recommends that EPA consider a refocus of research priorities in order to ensure sound health effects data are available in a timely fashion to better inform future CCL decision-making processes. The availability of this type of information will become increasingly important as issues such as pharmaceuticals and personal care products in drinking water continue to be of concern to the public.

Under the provisions of the SDWA the nation looks to EPA to set drinking water standards which are protective of the public's health. When adequate health effects research information is lacking, important regulatory determinations can be controversial and potentially misguided. Lacking EPA leadership on standard setting, states can be pressed into making independent regulatory determinations. In the case of perchlorate, at least two different drinking water standards have already been set by California and Massachusetts. In addition, Congress may also be compelled to by-pass the CCL process when inadequate health effects data results in controversial regulatory determinations.

Thank you for your consideration of this key recommendation on research needs. If you have any questions, please contact Veronica Blette, Designated Federal Officer for the NDWAC, at (202) 564-4094.

Sincerely, Gregg Grunenfelder Chair National Drinking Water Advisory Council

cc: Benjamin H. Grumbles, Assistant Administrator for Water George Gray, Assistant Administrator for Research and Development Cynthia C. Dougherty, Director,Office of Ground Water and Drinking Water Ephraim King, Director, Office of Science and Technology Kevin Teichman, Deputy Assistant Administrator for Research and Development EPA Docket ID No. EPA-HQ-OW-2008-0692

Response: EPA agrees that thorough health effects research can improve regulatory decision-making. We will continue to work with the NDWAC and other advisory groups to identify research needs for future decisions.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21103
EPA Comment Code: 1100

Comment: Finally, should a final determination be made not to establish a NPDWR for perchlorate, EPA should also make clear that its final determination also removes perchlorate from the CCL3 list. Based on EPA's careful consideration of the scientific evidence, it has fully evaluated perchlorate and met its requirements under the law. Continued consideration of perchlorate would siphon resources away from the long list of other substances and microbes on the CCL3.

X. References

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Clewell RA, Merrill EA, Gearhart JM, Robinson PJ, Sterner TR, Mattie DR, Clewell HJ 3rd. 2007. Perchlorate and radioiodide kinetics across life stages in the human: using PBPK models to predict dosimetry and thyroid inhibition and sensitive subpopulations based on developmental stage. J Toxicol Environ Health A 70:408-28.

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National Research Council of the National Academies (NAS). 2005. Health Implications of Perchlorate Ingestion. Committee to Assess the Health Implications of Perchlorate Ingestion, Board on Environmental Studies and Toxicology, Division on Earth and Life Studies. Washington, D.C.: The National Academies Press.

Tellez RT, Chacon PM, Abarca CR, Blount BC, Van Landingham CB, Crump KS, Gibbs JP. 2005. Longterm environmental exposure to perchlorate through drinking water and thyroid function during pregnancy and the neonatal period. Thyroid. 15(9):963-975.

Response: EPA has decided to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28793
EPA Comment Code: 1100

Comment: REGULATORY BACKGROUND

In 1974, Congress enacted the federal Safe Drinking Water Act (SDWA) to protect the public health from contaminated drinking water supplies by regulating public drinking water systems. The SDWA was amended in 1986 and 1994, and requires EPA, inter alia, to publish national primary drinking water regulations, which must include both non-enforceable, health-based Maximum Contaminant Level Goals (MCLGs) and enforceable Maximum Contaminant Levels (MCLs).[FN7: 42 U.S.C. [Sec] 300g-1(a)(1).] The MCLG must be set "at the level at which no known or anticipated adverse effects on the health of persons occur and which allows for an adequate margin of safety."[FN8: 42 U.S.C. [Sec]300g-1(b)(4)(A).] In contrast, the MCL, the maximum level of a regulated contaminant that any particular covered public water system may deliver to any user, must be set "as close to the maximum contaminant level goal as is feasible."[FN9: 42 U.S.C. [Sec]300g-1(b)(4)(B).] SDWA requires EPA to set a national primary drinking water standard when it determines for a contaminant that:

(i) the contaminant may have an adverse effect on the health of persons; (ii) the contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and (iii) in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.[FN10: 42 U.S.C. [Sec] 300g-1(b)(1)(A).]

SDWA also requires EPA to establish a "contaminant candidate list" (CCL) identifying a list of contaminants, not yet regulated by the Agency, which are known or anticipated to occur in drinking water and which may require regulation.[FN11: 42 U.S.C. [Sec]300g-1(b)(1)(B).] Every five years, EPA must determine whether or not to regulate five of the contaminants that appear on the CCL.[FN12: Id.]

In March, 1998, EPA's first CCL included perchlorate, but the Agency did not choose to make any determination about whether to regulate the contaminant. In February, 2005, EPA announced its second CCL, CCL2, on which perchlorate appeared again. As a result of its status as a candidate contaminant, EPA subsequently announced its preliminary determination not to regulate perchlorate in October, 2008.

Response: No response necessary to the information provided by the commenter.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28833
EPA Comment Code: 1100

Comment: Consideration For Future Regulations

The current regulatory framework in place in the US puts the burden on the government to show that a chemical is unsafe and must be regulated. This is a very slow process, which takes many years or even decades and often is done only after the presence of the specific chemical and its impacts have become well known. More importantly, the current process also lacks any incentive for chemical manufacturers to support source water protection, or to consider or disclose negative impacts of their products on human health and the natural environment and control the contaminants at generation points, which often would be much more economical than treating them at downstream water plants.

The issue is becoming a critical one as new analytical methods can detect ever- increasing contaminants of emerging concern at parts per trillion and below, and as potential treatment to remove them could significantly add to the financial burden of water utilities, their energy needs and greenhouse gas emissions.

These concerns can be resolved effectively and economically by a regulatory paradigm shift to put the lead responsibility where it belongs, i.e. on the generators of the contaminants. While it is not possible to address perchlorate in this way, in light of the new administration's reanalysis of the science of perchlorate, AMWA encourages this administration to also consider taking another look at how we can protect watersheds and drinking water quality by addressing preventable problems caused by the generators of chemicals and man-made sources of pollution.

Response: Please see response to comment code 7000.

EPA Comment Code: 1300 Length of the comment period following the October 2008 FR Notice

Response to Comment Code 1300: A number of commenters requested that EPA extend the 30 day comment period for the Agency's preliminary regulatory determination for perchlorate (73 FR 60262, October 10, 2008). In response to these comments, EPA extended the comment period until November 28, 2008, which provided commenters with 49 days to prepare comments. EPA received comment letters from over 37,000 individuals/ organizations on the October 2008 Federal Register Notice.

Individual Comments

Commenter Name: Jennifer Sass, PhD
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2008-0692-0322
EPA Comment ID: 19810
EPA Comment Code: 1300

Comment: Document ID: EPA-HQ-OW-2008-0692-EPA-HQ-OW-2008-0692-0322 Last Name: Sass, PhD First Name: Jennifer Title: Organization: Natural Resources Defense Council (NRDC) City: State: Zip Code: Phone Number: Fax Number: Country Code: Email Address: Current Category Code: 302

Comment:

October 17, 2008

Docket identification (ID): EPA-HQ-OW-2008-00692 Preliminary Regulatory Determination on Perchlorate

Re: Request for extension of comment period.

The October 10, 2008 Federal; Register notice announcing EPA.s preliminary regulatory determination on perchlorate opened the public comment period for 30 days, with comments due by November 10, 2008. Given the importance of the science on perchlorate and the exposure data, the Natural Resources Defense Council (NRDC) respectfully requests a 60-day extension of the public comment period to January 10, 2008 (that is, 90 days from the October 10, 2008 notice).

Response: See the response to comment code 1300.

Commenter Name: Jennifer Sass, PhD
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2008-0692-0322
EPA Comment ID: 19813
EPA Comment Code: 1300

Comment: Council (NRDC) respectfully requests a 60-day extension of the public comment period to January 10, 2008 (that is, 90 days from the October 10, 2008 notice).

EPA.s preliminary regulatory determination not to set a regulatory standard for perchlorate in drinking water could put 20 - 40 million people at risk for perchlorate toxicity, including infants, toddlers and pregnant women. A proposal with such far-reaching public health implications deserves careful and thorough comments with adequate time to review and respond to EPA.s analysis.

Part of EPA.s preliminary determination relies on perchlorate monitoring data from the Unregulated Contaminant Monitoring Rule. The large amount of occurrence data collected over five years from almost 4000 public water systems will require additional time for NRDC and other stakeholders to review and assess, especially in light of the importance EPA placed on these data in the preliminary determinations.

NRDC plans to submit public comments on this proposed determination, and a thoughtful and detailed technical response will require more than the 30 days that has been allotted by EPA. We respectfully request the comment period be extended by 60 days.

Response: See response to comment code 1300.

Commenter Name: Anila Jacob, M.D., M.P.H.
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-0466
EPA Comment ID: 19894
EPA Comment Code: 1300

Comment: October 22, 2008

Eric Burneson Office of Ground Water and Drinking Water Standards and Risk Management Division Environmental Protection Agency 1200 Pennsylvania Avenue, NW Washington, DC 20460

Re: Request for extension of comment period for Docket Identification (ID): EPA- HQ-OW- 2008-0692- Preliminary Regulatory Determination on Perchlorate

Dear Mr. Burneson:

EPA announced it's preliminary regulatory determination on perchlorate in the Federal Register notice dated October 10, 2008 and opened a public comment period for 30 days, with comments due by November 10, 2008. Given the far- reaching public health implications ofEPA's determination, the Environmental Working Group (EWG) plans to thoroughly review EPA's document and submit comments. The document that EPA has produced is 80 pages long and highly technical and EWG respectfully requests that the comment period be extended by 60 days, so comments will be due 90 days from the October 10, 2008 notice.

Response: See response to comment code 1300.

Commenter Name: Anila Jacob, M.D., M.P.H.

Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-0466
EPA Comment ID: 19895
EPA Comment Code: 1300

Comment: Perchlorate contamination of drinking water potentially affects 20 to 40 million US. residents and EPA's preliminary regulatory determination not to regulate perchlorate has serious health implication for these millions of people. A thorough and detailed response to EPA's determination will require EWG scientists to pore qver EPA's document line by line in order to effectively make our argument for stringent regulation of perchlorate in drinking water. As advocates for public health, EWG has a responsibility to submit the strongest document to EPA that we can and we feel that an extension of the public comment period by 60 days will allow us to do that.

Thank you for your consideration. Best regards, Anila Jacob, M.D., M.P.H. Senior Scientist Environmental Working Group

Response: See the response to comment code 1300.

Commenter Name: Apparent Mass Mailing #3 Group Unidentified
EPA Document ID: EPA-HQ-OW-2008-0692-0561
EPA Comment ID: 19964
EPA Comment Code: 1300

Comment: Docket Identification (ID) Number: EPA-HQ-OW-2008-0692 Preliminary Regulatory Determination on Perchlorate Re: Request for extension of comment period

I am writing to express my concern regarding the EPA's failure to regulate perchlorate, as well as the proposed reference level, which fails to protect - and will adversely affect -- the health and development of hundreds of thousands, perhaps millions of American children.

EPA has spent a number of years researching perchlorate and developing its conclusions - which are considered highly controversial and complex. They require, therefore, the time for measured and throughful public response.

We cannot afford to have this decision rushed through, in the last days of the current administration, and leaving those communities that face the greatest risk without enough time to comment.

It takes time for public and community groups to evaluate EPA's findings, review the ever-changing scientific literature, and prepare comments.

I therefore request that the EPA extend the 30-day comment period on its October 10, 2008 Preliminary Regulatory Determination on Perchlorate to 90 days.

Response: See the response to comment code 1300. EPA plans to initiate the process of proposing a national primary drinking water regulation for perchlorate (see response to comment code 6120).

Commenter Name: Apparent Mass Mailing #3 Group Unidentified
EPA Document ID: EPA-HQ-OW-2008-0692-0561
EPA Comment ID: 19964
EPA Comment Code: 1300

Comment: Docket Identification (ID) Number: EPA-HQ-OW-2008-0692 Preliminary Regulatory Determination on Perchlorate Re: Request for extension of comment period

I am writing to express my concern regarding the EPA's failure to regulate perchlorate, as well as the proposed reference level, which fails to protect - and will adversely affect -- the health and development of hundreds of thousands, perhaps millions of American children.

EPA has spent a number of years researching perchlorate and developing its conclusions - which are considered highly controversial and complex. They require, therefore, the time for measured and throughful public response.

We cannot afford to have this decision rushed through, in the last days of the current administration, and leaving those communities that face the greatest risk without enough time to comment.

It takes time for public and community groups to evaluate EPA's findings, review the ever-changing scientific literature, and prepare comments.

I therefore request that the EPA extend the 30-day comment period on its October 10, 2008 Preliminary Regulatory Determination on Perchlorate to 90 days.

Response: See the response to comment code 1300. EPA plans to initiate the process of proposing a national primary drinking water regulation for perchlorate (see response to comment code 6120).

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0585
EPA Comment ID: 19968
EPA Comment Code: 1300

Comment: time to comment should be extended. i want very much to hear what environmental working group comments. i trust them more than my own government agencies. and certainly more than profiteers.

Response: See the response to comment code 1300.

Commenter Name: S. Quezada
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0596
EPA Comment ID: 19971
EPA Comment Code: 1300

Comment: Docket Identification (ID) Number: EPA-HQ-OW-2008-0692 Preliminary Regulatory Determination on Perchlorate Re: Request for extension of comment period

Americans cannot afford to have a final determination on Perchlorate's safety rushed through in light of the high scientific controversy surrounding the matter. Therefore, I request an extension of public comments from 30 days to 90 days. This action by the EPA would be appropriate and prudent given the high scientific and academic controversy over the matter. Even the mere appearance of "rushing" is in appropriate and should be dispelled by providing Americans the opportunity to fully evaluate and meaningfully comment on the EPA's proposed perchlorate determination.

The EPA has spent a number of years researching perchlorate and developing its conclusions. To now turn around and provide the American public 30 days for public comment on a complex matter is both unfair and questionable and certainly not aimed at obtaining "public comment."

Sincerely,

S. Quezada

416 Ridgeview Ave

Iowa City, Iowa 52246

Response: See the response to comment code 1300.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0629
EPA Comment ID: 19980
EPA Comment Code: 1300

Comment: Docket Identification (ID) Number: EPA-HQ-OW-2008-0692 Preliminary Regulatory Determination on Perchlorate Re: Request for extension of comment period

To Whom It May Concern:

It is clear that the issue of how/whether to regulate perchlorate is not a simply resolved one. Please extend the comment period on the October 10, 2008 Preliminary Regulatory Determination on Perchlorate to at least 90 days, so that as many entities with views and knowledge of the subject as possible may have a chance to be heard. The benefits of extending seem certain to outweigh any negatives that might be involved in doing so.

Response: See the response to comment code 1300.

Commenter Name: N Henry
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0637
EPA Comment ID: 19984

EPA Comment Code: 1300

Comment: Please extend the comment period regarding perchlorate regulation. The quality of our water supply and health of our nation are serious matters, which require appropriate deliberation and evaluation.

Thank you.

Response: See the response to comment code 1300.

Commenter Name: Lenny Siegel
Commenter Organization: Center for Public Environmental Oversight
EPA Document ID: EPA-HQ-OW-2008-0692-0642
EPA Comment ID: 19985
EPA Comment Code: 1300

Comment: Attachments

EPA-HQ-OW-2008-0692-0642.1 Comment attachment submitted by Lenny Siegel, Executive Director, Center for Public Environmental Oversight

Eric Burneson Office of Ground Water and Drinking Water Standards and Risk Management U.S. Environmental Protection Agency

REF: Docket ID# EPA-HQ-OW-2008-0068

Dear Sir:

I am concerned that EPA's failure to regulate perchlorate, as well as its unprotective proposed health reference level, will adversely affect the health and development of hundreds of thousands, perhaps millions of American children. It has taken EPA years, with its extensive resources, to come to its conclusions. Its findings are complex and controversial. We cannot afford to have this decision rushed out the door, in the waning days of the current administration, without giving impacted communities sufficient time to comment.

Organizations that advocate for public health and environmental protection have few people with the expertise, resources, and time to evaluate EPA's findings, review continuously emerging scientific literature, and prepare comments. I therefore call upon EPA to extend the 30-day comment period on its October 10, 2008 Preliminary Regulatory Determination on Perchlorate to 90 days.

Sincerely,

(submitted electronically)

Lenny Siegel Executive Director

Cc: EPA Administrator Stephen Johnson

Response: See the response to comment code 1300. EPA plans to initiate the process of proposing a national primary drinking water regulation for perchlorate (see response to comment code 6120).

Commenter Name: Caroline Baier-Anderson, PhD
Commenter Organization: Health Scientist, Environmental Defense Fund PUBLIC
EPA Document ID: EPA-HQ-OW-2008-0692-0649
EPA Comment ID: 19992
EPA Comment Code: 1300

Comment: October 27, 2008

Mr. Eric Burneson Office of Ground Water and Drinking Water Standards and Risk Management Division Environmental Protection Agency 1200 Pennsylvania Avenue, NW Washington, DC 20460 Re: Request for extension of comment period for Docket Identification (ID): EPA- HQ-OW-2008- 0692- Preliminary Regulatory Determination on Perchlorate

Dear Mr. Burneson:

On October 10, 2008, EPA published a Federal Register notice announcing the opening of a 30-day comment period on its preliminary regulatory determination on perchlorate. We have concerns regarding the proposed regulatory determination, in particular the unprecedented use of a pharmacodynamic model to justify the exceedance of the reference dose and we believe this introduces complexity into the evaluation of the standard that merits more than just 30 days for judicious scientifically-sound public comment. We therefore request that the comment period be extended by 60 days, so comments will be due 90 days from the October 10, 2008 notice, on January 10, 2009.

Thank you for considering this request.

Sincerely, Caroline Baier-Anderson, Ph.D. Health Scientist

Response: See the response to comment code 1300.

Commenter Name: Luis Olmedo Vélez
Commenter Organization: Comité Cívico del Valle, Inc.
EPA Document ID: EPA-HQ-OW-2008-0692-0652
EPA Comment ID: 19995
EPA Comment Code: 1300

Comment: Among profit and non-profit organizations that take environmental issues seriously, there are only several people who are qualified to measure and evaluate EPA'S findings and conclusions. Therefore, a 30-day comment period is far too short a time period to take action against any rulings that may be detrimental to the water supply. We ask that the EPA extend the preliminary regulatory determination date to 90-days.

Sincerely,

Luis Olmedo Vélez Executive Director Comité Cívico del Valle, Inc. Center for Health Education, Prevention and Advocacy

Response: See the response to comment code 1300.

Commenter Name: Steven Brittle
Commenter Organization: Don't Waste Arizona
EPA Document ID: EPA-HQ-OW-2008-0692-0653
EPA Comment ID: 19996
EPA Comment Code: 1300

Comment: October 26, 2008

Eric Burneson Office of Ground Water and Drinking Water Standards and Risk Management U.S. Environmental Protection Agency Ariel Rios Building 1200 Pennsylvania Avenue, N. W. Mail Code: 4607M Washington, DC 20460

Dear Sir:

Don't Waste Arizona (DWAZ) is a non-profit environmental organization especially concerned about toxics issues.

DWAZ is concerned that EPA's failure to regulate perchlorate, as well as its unprotective proposed health reference level, will adversely affect the health and development of hundreds of thousands, perhaps millions of American children, including those in Arizona. It has taken EPA years, with its extensive resources, to come to its conclusions. Its findings are complex and controversial. We cannot afford to have this decision rushed out the door, in the waning days of the current administration, without giving impacted communities sufficient time to comment.

Organizations that advocate for public health and environmental protection have few people with the expertise, resources, and time to evaluate EPA's findings, review continuously emerging scientific literature, and prepare comments. DWAZ therefore calls upon EPA to extend the 30-day comment period on its October 10, 2008 Preliminary Regulatory Determination on Perchlorate to 90 days.

Sincerely,

Stephen M Brittle President Don't Waste Arizona 6205 South 12th Street Phoenix, AZ 85042 602-268-6110

Cc: EPA Administrator Stephen Johnson

Response: See the response to comment code 1300. EPA plans to initiate the process of proposing a national primary drinking water regulation for perchlorate (see response to comment code 6120).

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0682

EPA Comment ID: 20023
EPA Comment Code: 1300

Comment: I request the comment period be extended for 90 days to give those a chance to review the information and offer their voice about it. re. the regulatory determination on PERCHLORATE.....epa -hq--ow-2008-0692

Response: See the response to comment code 1300.

Commenter Name: Luis Olmedo Vélez
Commenter Organization: Comité Cívico del Valle, Inc., Center for Health Education, Prevention and Advocacy
EPA Document ID: EPA-HQ-OW-2008-0692-0736
EPA Comment ID: 20048
EPA Comment Code: 1300

Comment: Among profit and non-profit organizations that take environmental issues seriously, there are only several people who are qualified to measure and evaluate EPA'S findings and conclusions. Therefore, a 30-day comment period is far too short a time period to take action against any rulings that may be detrimental to the water supply. We ask that the EPA extend the preliminary regulatory determination date to 90-days.

Sincerely,

Luis Olmedo Vélez Executive Director Comité Cívico del Valle, Inc. Center for Health Education, Prevention and Advocacy

Response: See the response to comment code 1300.

Commenter Name: Lynn and Paul Thorp and Schwartz
Commenter Organization: Clean Water Action (CWA)
EPA Document ID: EPA-HQ-OW-2008-0692-0750
EPA Comment ID: 20056
EPA Comment Code: 1300

Comment: October 28, 2008 Eric Burneson U.S. Environmental Protection Agency Arid Rios Building 120o Pennsylvania Ave. NW Washington DC 20460 Re: Request for Extension of Comment Period for Preliminary Regulatory Determination on Perchlorate Public Noticed October to, 2008 at 73 Fed. Reg. 60262 Docket Identification (ID): EPA-HQ-OW-2008-00692

Dear Mr. Burneson: On behalf of our more than 1.2 million members, we request an extension of the public comment period for the Preliminary Regulatory Determination on Perchlorate of at least 60 days beyond the November to deadline, for a total extension of not less than qo days to January to, 2009. The proposed Preliminary Regulatory Determination on Perchlorate raises complex issues which require more time to be sufficiently reviewed. Furthermore, the Determination makes conclusions which contradict those made by several states, such as Massachusetts and New Jersey, which have reviewed the same issue and have set a drinking water standard for percblorate. The Determination raises serious implications for human health. These include the exposure to

perchlorate by millions of Americans in their food and the adverse effects of perchlorate exposure to those most at risk, including infants, toddlers, and pregnant women. Additional time will enable us to analyze and make informed comments regarding the Preliminary Determination. Please make this letter part of the comment record for the Preliminary Determination. Thank you for your attention to this request.

Sincerely,

Lyn Thorp National Campaign Coordinator Ext. 109

Paul Schwartz National Policy Coordinator Ext. 105

CC: Stephen Johnson, Administrator, US Environmental Protection Agency [Via First Class Mail and Fax 202-501-1450]

Response: See the response to comment code 1300.

Commenter Name: Robin Mark Freeman
Commenter Organization: Merritt College
EPA Document ID: EPA-HQ-OW-2008-0692-0662
EPA Comment ID: 20237
EPA Comment Code: 1300

Comment: Organizations that advocate for public health and environmental protection have few people with the expertise, resources, and time to evaluate EPA's findings, review continuously emerging scientific literature, and prepare comments. We therefore call upon EPA to extend the 30-day comment period on its October 10, 2008 Preliminary Regulatory Determination on Perchlorate to 90 days.

Sincerely, Prof. Robin Mark Freeman, Co-Director Institute for Sustainable Policy Studies Merritt College, Oakland , CA

Cc: EPA Administrator Stephen Johnson

Response: See the response to comment code 1300.

Commenter Name: Tatjana and Jeremy Thomas
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0669
EPA Comment ID: 20243
EPA Comment Code: 1300

Comment: Water Docket Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Ave., NW Washington, DC 20460

Docket Identification (ID) Number: EPA-HQ-OW-2008-0692 Preliminary Regulatory Determination on Perchlorate Re: Request for extension of comment period

I am writing to express my concern regarding the EPA's failure to regulate perchlorate, as well as the proposed reference level, which fails to protect - and will adversely affect -- the health and development of hundreds of thousands, perhaps millions of American children.

EPA has spent a number of years researching perchlorate and developing its conclusions - which are considered highly controversial and complex. They require, therefore, the time for measured and throughful public response.

We cannot afford to have this decision rushed through, in the last days of the current administration, and leaving those communities that face the greatest risk without enough time to comment.

It takes time for public and community groups to evaluate EPA's findings, review the ever-changing scientific literature, and prepare comments.

I therefore request that the Sincerely, EPA extend the 30-day comment period on its October 10, 2008 Preliminary Regulatory Determination on Perchlorate to 90 days.

Sincerely,

Tatjana Thomas

Response: See the response to comment code 1300. EPA plans to initiate the process of proposing a national primary drinking water regulation for perchlorate (see response to comment code 6120).

Commenter Name: D. Manzullo
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0676
EPA Comment ID: 20250
EPA Comment Code: 1300

Comment: Allow more time for all the appropriate researchers and scientists to comment on the harm these chemicals are doing to humans, living creatures and plant life!

Response: See the response to comment code 1300.

Commenter Name: S. Smolen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0679
EPA Comment ID: 20255
EPA Comment Code: 1300

Comment: Because the decision of whether or not to implement a national maximum contaminant level is so important and far reaching, I respectfully request that the EPA extend the comment period to 90+ days (an additional 60 days past the current deadline of November 10th) in order to

allow groups wishing to submit comments on the decision sufficient time to review and respond to the evidence supporting the EPA's position.

Sincerely,

Stephanie Smolen Former San Gabriel Valley resident EPA Region 9, Superfund Areas 1 & 2, California EPA ID#'s CAD980677355 & CAD980818512 respectively

Response: See the response to comment code 1300.

Commenter Name: Kathy M. Kinsey
Commenter Organization: Maryland Department of the Environment
EPA Document ID: EPA-HQ-OW-2008-0692-1421
EPA Comment ID: 20426
EPA Comment Code: 1300

Comment: Kathy M. Kinsey Senior Policy Advisor Maryland Department of the Environment 410-537-3897 kkinsey@mde.state.md.us Re: Docket ID No. EPA-HQ-OW-2008-0692 Comments on Perchlorate Determination November 7, 2008

The Maryland Department of the Environment ("Department") submits the following comments on EPA's preliminary regulatory determination on perchlorate.

Request for Extension of the Public Comment Period

As a preliminary matter, the Department requests that EPA extend the public comment period. EPA's preliminary determination not to set a regulatory standard for perchlorate in drinking water has serious public health implications for the millions of people potentially exposed to perchlorate through public drinking water systems. EPA's determination was based on an analysis of highly complex data and an unprecedented application of published models with adjustments that have not undergone peer review. A thorough and thoughtful review of EPA's analysis and preliminary determination requires more than the 30 days currently allotted by EPA. The Department, therefore, requests that EPA extend the public comment period by a minimum of 60 days beyond the current November 10, 2008 deadline for submitting comments.

Response: See the response to comment code 1300.

Commenter Name: Kathy M. Kinsey
Commenter Organization: Maryland Department of the Environment
EPA Document ID: EPA-HQ-OW-2008-0692-1421
EPA Comment ID: 20429
EPA Comment Code: 1300

Comment: For the foregoing reasons, the Department urges EPA to both extend the public comment period on its preliminary determination by an additional 60 days beyond the current November 10, 2008 deadline, and set a federal drinking water standard for perchlorate.

Response: See the response to comment code 1300.

Commenter Name: Vicky and Bll Clary
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0622
EPA Comment ID: 20465
EPA Comment Code: 1300

Comment: EPA has spent a number of years researching perchlorate and developing its conclusions - which are considered highly controversial and complex. They require, therefore, the time for measured and throughful public response.

We cannot afford to have this decision rushed through, in the last days of the current administration, and leaving those communities that face the greatest risk without enough time to comment. Every American affected should have a voice in this issue and it shouldn't be decided by the military or pushed through before we are all given a chance to comment or even to become aware of the problem.

It takes time for public and community groups to evaluate EPA's findings, review the ever-changing scientific literature, and prepare comments.

I therefore request that the EPA extend the 30-day comment period on its October 10, 2008 Preliminary Regulatory Determination on Perchlorate to 90 days.

Sincerely,

Vicky and Bll Clary

Response: See the response to comment code 1300.

Commenter Name: Nancy Yoke
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0621
EPA Comment ID: 20560
EPA Comment Code: 1300

Comment: I am writing to express my concern regarding the EPA's failure to regulate perchlorate, as well as the proposed reference level, which fails to protect - and will adversely affect -- the health and development of hundreds of thousands, perhaps millions of American children.

EPA has spent a number of years researching perchlorate and developing its conclusions - which are considered highly controversial and complex. They require, therefore, the time for measured and throughful public response.

We cannot afford to have this decision rushed through, in the last days of the current administration, and leaving those communities that face the greatest risk without enough time to comment.

It takes time for public and community groups to evaluate EPA's findings, review the ever-changing scientific literature, and prepare comments.

I therefore request that the EPA extend the 30-day comment period on its October 10, 2008 Preliminary Regulatory Determination on Perchlorate to 90 days.

Sincerely,

Nancy Yoke

Response: See the response to comment code 1300. EPA plans to initiate the process of proposing a national primary drinking water regulation for perchlorate (see response to comment code 6120).

Commenter Name: Caroline Baier-Anderson
Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1534
EPA Comment ID: 20637
EPA Comment Code: 1300

Comment: November 13, 2008

Mr. Eric Burneson Office of Ground Water and Drinking Water Standards and Risk Management Division Environmental Protection Agency 1200 Pennsylvania Avenue, NW Washington, DC 20460

Re: Second request for extension of comment period for Preliminary Regulatory Determination on Perchlorate, Docket ID EPA-HQ-OW-2008-0692

Dear Mr. Burneson:

On October 10, 2008, EPA published a Federal Register notice announcing the opening of a 30-day comment period on its preliminary regulatory determination on perchlorate and on October 27th we submitted to the docket a letter requesting that the comment period be extended for 60 days (EPA-HQ- OW-2008-0692-0649). On November 7, EDF was notified by telephone that the comment period has been extended only 18 days, until November 28, 2008, but that the notice for this extension would not be entered into the Federal Register until Wednesday, November 12, two days after the initial deadline for comments.

We believe that this extension is inadequate, for the following reasons:

1. As noted in our previous letter, the Preliminary Regulatory Determination on Perchlorate is based on the virtually unprecedented use of a pharmacodynamic model developed by industry to justify the exceedance of the reference dose. This model and its novel application introduce significant complexity into the evaluation of the standard, which merits more than just 30 days for judicious scientifically-sound public comment.

2. Providing only an 18-day extension to this comment period is far shorter than and hence not consistent with other extensions EPA has granted. For example:

* Three extensions were made to the comment period for the "Draft List of Initial Pesticide Active Ingredients and Pesticide Inerts to be Considered for Screening under the Federal Food, Drug, and Cosmetic Act", consisting of 60 days, 45 days, and 42 days, for a total of 147 days (EPA-HQ-OPPT-2004-0109; FRL-8346-5).

* The comment period for the re-registration of Chloropicrin, Dazomet, Metam Sodium/Potassium, and Methyl Bromide was extended for 45 days (EPA-HQ- OPP-2008-0518; FRL-8380-5).

* The comment period for the "Proposed Rule for Standards of Performance for Portland Cement Plants" was also extended by 45 days (EPA-HQ-OAR-2008-0260; FRL-8703-2).

3. Since presumably you could only contact those commenters whom you knew or anticipated were planning to submit comments, the failure to post the notice of the extension in a timely manner placed any commenters not known to you at a significant disadvantage. (An incorrect docket number published in the initial notice also likely serves to further confuse and delay commenters.)

We therefore reiterate our request that the comment period be extended by at least 60 days, with comments due no earlier than 90 days from the October 10, 2008 notice, or January 10, 2009. We consider this request to be both reasonable and justified by the complexity of and importance of the decision. It is also more in line with other extensions the Agency has granted.

We request a reply at your earliest convenience.

Thank you again for your consideration.

Sincerely,

Caroline Baier-Anderson, Ph.D. Health Scientist

Response: EPA considered this request for a second extension beyond the revised November 28, 2008 extension but concluded that a further extension beyond the 49 days provided was not needed for commenters to consider the information in the 1 page Federal Register Notice and would unnecessarily delay decision making.

Commenter Name: Deborah Swackhamer
Commenter Organization: Science Advisory Board
EPA Document ID: EPA-HQ-OW-2008-0692-1749
EPA Comment ID: 20660
EPA Comment Code: 1300

Comment: As you know, the SAB operates under the requirements of the Federal Advisory Committee Act for advance notice of public meetings. Therefore, the SAB will not be able to provide you with our comments regarding the scientific basis of this determination in time to meet the Agency's deadline of November 10, 2008. Accordingly, the SAB urges the Agency to consider extending the public comment period thereby allowing us to provide comments for the Agency's consideration in making the final regulatory determination on perchlorate. Thank you in advance for your consideration.

Sincerely,

/Signed/ Dr. Deborah L. Swackhamer, Chair Science Advisory Board

/Signed/ Dr. Joan Rose, Chair SAB Drinking Water Committee

cc: Marcus Peacock, Deputy Administrator Ben Grumbles, Assistant Administrator, Office of Water Cynthia Dougherty, Office of Water

Response: Administrator Stephen Johnson replied to the SAB on January 9, 2009. The letter is available in EPA's docket ID No. EPA-HQ-OW-2009-0297 for this notice

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Commenter Name: S. Quezada
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1840
EPA Comment ID: 20729
EPA Comment Code: 1300

Comment: October 24, 2008 Water Docket Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Ave., NW Washington, DC 20460

Docket Identification (ID) Number: EPA-HQ-OW-2008-0692 Preliminary Regulatory Determination on Perchlorate Re: Request for extension of comment period

Americans cannot afford to have a final determination on perchlorate's safety rushed through in light of the high scientific controversy surrounding the matter. Therefore, I request an extension of public comments from 30 days to 90 days. This extension would be appropriate and prudent given the high scientific and academic controversy over the matter. Even the mere appearance of "rushing" to a final determination is inappropriate and should be dispelled by providing Americans the opportunity to fully evaluate and meaningfully comment on the EPA's proposed action.

The EPA has spent a number of years researching perchlorate and developing its conclusions. To now, turn around and provide the American public 30 days for public comment on a complex matter is both unfair and questionable as to whether the EPA truly seeks to obtain the public's comments (to which the EPA must articulate a rational response in its final adoption of any perchlorate's final determination).

Sincerely, S. Quezada 416 Ridgeview Ave Iowa City, Iowa 52246

Response: See the response to comment code 1300.

Commenter Name: Andrew E. Stevenson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1878
EPA Comment ID: 20766
EPA Comment Code: 1300

Comment: Please extend the public comment for this important environmental issue, in order to give the citizens of our country time to weigh in on this.

Sincerely yours, Andrew E. Stevenson 311-A East Bellefonte Ave. Alexandria, VA 22301

Response: See the response to comment code 1300.

Commenter Name: Mary Moore
Commenter Organization: Lindon Park Neighborhood Association (LPNA)
EPA Document ID: EPA-HQ-OW-2008-0692-2002
EPA Comment ID: 20833
EPA Comment Code: 1300

Comment: U.S. Environmental Protection Agency Office of Water Docket (Mail Code: 2822T) 1200 Pennsylvania Ave., NW Washington, DC 20460

Ref: Docket EPA-HQ-OW-2008-068 Drinking Water: Preliminary Regulatory Determination on Perchlorate

To Whom It May Concern:

The Lindon Park Neighborhood Association (LPNA) respectfully requests that EPA extend the public comment period for 60 days to allow sufficient time for a thorough review of the documents used by EPA in reaching the preliminary determination not to issue a national primary drinking water regulation.

Response: See the response to comment code 1300.

Commenter Name: D'Lanie Blaze
Commenter Organization: TheAeroSpace
EPA Document ID: EPA-HQ-OW-2008-0692-0641
EPA Comment ID: 20892
EPA Comment Code: 1300

Comment: It the EPA is indeed motivated by an ethical commitment to safety, it will recognize the error in this decision. It will also facilitate public awareness and extend an obvious invitation to take part in this process, recognizing that 90+ days is required for the public to exercise this right in an informed capacity.

Sincerely,

D'Lanie Blaze Mission Control : TheAeroSpace IGNITE YOUR INTELLECT : CONNECT!

http://www.TheAeroSpace.org

Links of Interest : SSFL

http://www.ACMELA.org http://www.RocketdyneArchives.com http://www.dtsc-ssfl.com/ http://www.CleanUpRocketdyne.org http://www.CommitteeToBridgeTheGap.org

Response: See the response to comment code 1300.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20918
EPA Comment Code: 1300

Comment: In light of the extremely short initial public comment period of 30 days and the complexity of the EPA assessment, EWG and other environmental groups requested a 60- day extension of the comment period. On November 10th, EPA granted an 18-day extension to the initial comment period. EWG respectfully requests that the 60- day extension that we had initially requested be granted to allow for a more thorough review of EPA's assessment.

Response: See the response to comment code 1300.

Commenter Name: Ron Curry
Commenter Organization: New Mexico Environment Department
EPA Document ID: EPA-HQ-OW-2008-0692-1796
EPA Comment ID: 20930
EPA Comment Code: 1300

Comment: November 26, 2008

Stephen L. Johnson Administrator United States Environmental Protection Agency c/o Water Docket Mailcode 2822T 1200 Pennsylvania, N.W. Washington, D.C. 20460

Re:Comments on Preliminary Regulatory Determination on Perchlorate Docket ID No. EPA-HQ-OW-2008-0692

Dear Administrator Johnson:

By this letter I am submitting the comments of the New Mexico Environment Department on the Preliminary Determination on Perchlorate that the United States Environmental Protection Agency (EPA) issued on October 3, 2008. 73 Fed. Reg. 60262 (Oct.10, 2008). Although EPA initially requested comments by November 10, 2008, the agency subsequently extended the comment period through November 28, 2008. 73 Fed. Reg. 66895 (Nov. 12, 2008). The Environment Department appreciates the opportunity to comment on this important regulatory decision, and the extension of time to submit these comments.

Response: No response necessary to the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855

EPA Comment ID: 21091
EPA Comment Code: 1300

Comment: II. The EPA Should Publish its Final Determination as Soon as Possible

In the Federal Register notice, EPA has set a timeline for public comment, a final decision, and the possible decision to set a Health Advisory (HA). EPA's timeline for a final determination is wise for two principal reasons. First, the 45-day period provides ample time for the public to review EPA documents and submit comments as EPA has offered substantial opportunities for public comment on this matter. EPA previously provided a 60-day public comment period on the Contaminant Candidate List 2 (CCL) preliminary regulatory determinations for 11 chemicals issued May 1, 2007 via publication in the Federal Register as well as on its website.[FN1: 72 Fed. Reg. 24016 (2007) (published May 1, 2007).] In that publication, EPA also extended the opportunity to the public to comment on perchlorate. The PSG and other organizations commented extensively on that notice. EPA, indicating it was not issuing a determination at that time, discussed the various scientific and technical data being reviewed and considered by the agency, including the National Academy of Sciences (NAS) report, the Unregulated Contaminant Monitoring Rule 1 (UCMR) occurrence data, and options to use data to establish the relative source contribution (RSC). The agency also identified options for potential methodologies that could be employed to make a determination, including the option of using the NHANES and UCMR 1 data. EPA has selected that approach as its basis for its preliminary determination. Thus EPA has offered the public multiple opportunities for public comment, more than most substances on the CCL for which EPA has made a determination.

Response: See the response to comment code 1300.

Commenter Name: Teresa Jordan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2086
EPA Comment ID: 21109
EPA Comment Code: 1300

Comment: Mr. Grumbles and Mr. Burneson, I thank the USEPA, and persons who may have made the request, for extending the public comment period. I had not written sooner because I have had my hands full adressing: California State Water Resources Control Board water issues, the Los Angeles Regional Water Quality Control Board's Basin Plan Triennial Review, the California 2009 Water Plan Update (Initial, Working, and Pre-Administrative Draft Plans for the South Coast Hydrologic Region-Ventura and Los Angeles Counties), and Alaska's Seafood Processors general NPDES Permit.

Sincerely,

Mrs. Teresa Jordan

[see attachments Docket ID EPA-HQ-OW-208-0692-2086]

Response: No response necessary to the information provided by the commenter.

EPA Comment Code: 1500 EPA's handling of comments on the October 2008 FR Notice

Individual Comments

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection (MassDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0495
EPA Comment ID: 28858
EPA Comment Code: 1500

Comment: Docket ID No. EPA-HQ-OW-2009-0297 Drinking Water: Perchlorate Supplemental Request for Comments. U.S. Environmental Protection Agency.

The Massachusetts Department of Environmental Protection Office of Research and Standards is pleased to provide the attached comments regarding the U.S. Environmental Protection Agency's (EPA) decision to reconsider its approach to analyzing scientific data related to perchlorate in drinking water. The Wednesday, August 19, 2009 Federal Register announcement includes a summary of the major comments EPA received regarding its October 10, 2008 preliminary regulatory determination to not regulate perchlorate in drinking water. This includes comments on why the proposed 15 ppb health advisory is not protective of children's health. These comments provide a strong basis for EPA's appropriate decision to consider a broader range of alternatives for interpreting the health data, the level of health concern, the frequency of occurrence of perchlorate in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard. The Commonwealth of Massachusetts' Department of Environmental Protection (MassDEP) is pleased to provide comments on several of the issues that are the focus of this Federal Register announcement and is available to further consult with you or answer any questions you may have on our comments. Our comments are organized by issues described in specific sections of the Federal Register and are detailed in the attachment. Thank you.

Attachment

September 17, 2009

Docket ID No. EPA-HQ-OW-2009-0297 Drinking Water: Perchlorate Supplemental Request for Comments U.S. Environmental Protection Agency

We highly commend the U.S. Environmental Protection Agency's (EPA) decision to reconsider its approach to analyzing scientific data related to perchlorate in drinking water. The Wednesday, August 19, 2009 Federal Register announcement includes a summary of the major comments EPA received regarding its October 10, 2008 preliminary regulatory determination to not regulate perchlorate in drinking water. This includes comments on why the proposed 15 ppb health advisory is not protective of children's health. These comments provide a strong basis for EPA's appropriate decision to consider a broader range of alternatives for interpreting the health data, the level of health concern, the frequency of occurrence of perchlorate in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard. The Commonwealth of

Massachusetts' Department of Environmental Protection (MassDEP) is pleased to provide comments on several of the issues that are the focus of this Federal Register announcement and is available to further consult with you or answer any questions you may have on our comments. Our comments are organized by issues described in specific sections of the Federal Register.

Response: No response is necessary to the information provided by the commenter.

EPA Comment Code: 1600 Length of the comment period following August 2009 FR Notice

Response to Comment Code 1600: A number of commenters requested an extension to EPA's 30 day comment period on the Agency's August 19, 2009 Federal Register Notice (74 FR 41883, August 19, 2009). In response to these requests, the Agency extended the comment period until October 8, 2009, thereby providing commenters with 51 days to review the information contained in the Federal Register Notice and prepare comments. EPA received comment letters from over 6,000 individuals and organizations on the August 19, 2009 Federal Register Notice.

Individual Comments

Commenter Name: David L. Thomas
Commenter Organization: National Sorghum Producers
EPA Document ID: EPA-HQ-OW-2009-0297-0336
EPA Comment ID: 28447
EPA Comment Code: 1600

Comment: September 14, 2009

Eric Burneson Office of Ground Water and Drinking Water Standards and Risk Management Division Environmental Protection Agency 1200 Pennsylvania Avenue, NW Washington, DC 20460

Re: Request for extension of comment period for Docket Identification (ID) EPA- HQ-OW-2008-0692-Perchlorate Supplemental Request for Comments

Dear Mr. Burneson,

In the Federal Register on August 19, 2009, EPA published a notice seeking comments under a 30 day public comment period on "additional approaches available for analyzing data related to EPA's perchlorate regulatory determination."

The sorghum industry has been using the chemical perchlorate for many years. It is essential to producers because it aids in the dry down process and allows crops to be harvested properly without additional moisture.

Even though perchlorate is naturally occurring, EPA states in the August 19, 2009 Federal Register notice that the "additional alternatives under consideration could result in health reference levels which are much lower than the level identified in the October 2008 notice."

Since the public comments collected under this Federal register could have serious affects on sorghum producers, the National Sorghum Producers asks that EPA establish the appropriate science based methodology before proceeding with a regulatory determination. EPA has raised a number of complicated scientific issues in this Federal Register notice that will impact our

producers. On their behalf, we are requesting that the comment period be extended by 60 days to allow for a more thorough analysis of the issues raised.

Thank you for your consideration.

Sincerely, David L. Thomas

Response: See response to comment code 1600.

Commenter Name: Larry Cummings
Commenter Organization: Perchlorate Study Group (PSG)
EPA Document ID: EPA-HQ-OW-2009-0297-0417
EPA Comment ID: 28471
EPA Comment Code: 1600

Comment: The Perchlorate Study Group acknowledges that EPA has placed a notice on their website granting a 15-day extension to the comment period for Docket EPA-HQ- OW-2009-0297 and intends to submit detailed comments by the conclusion of the extension.

September 18, 2009

U.S. Environmental Protection Agency Office of Water Docket (Mailcode 2822T) 1200 Pennsylvania Avenue, NW Washington, DC 20460

Re: Comments in Response to EPA Drinking Water: Perchlorate Supplemental Request for Comments [EPA-HQ-OW-2009-0297]

The Perchlorate Study Group (PSG) acknowledges that EPA has posted on its website a statement that the comment period for Docket EPA-HQ-OW-2009-0297 has been extended for a period of 15 days. This action will allow us to submit more detailed responses to the questions that have been raised in the August 19 "Drinking Water: Perchlorate Supplemental Request for Comments" for EPA's consideration. We look forward to receiving formal notice of this action next week and will submit our comments by the 15-day closing date provided in the Federal Register notice announcing the extension of the comment period.

We welcome the opportunity to meet with EPA staff to explain our position in greater detail. Please feel free to contact me at 3883 Howard Hughes Parkway, Suite 700, Las Vegas, NV 89169.

Sincerely, Larry Cummings Chairman Perchlorate Study Group

Response: No response necessary to the information provided by the commenter.

Commenter Name: Stephen Haterius
Commenter Organization: The National Association of State Departments of Agriculture (NASDA)
EPA Document ID: EPA-HQ-OW-2009-0297-0500
EPA Comment ID: 28484
EPA Comment Code: 1600

Comment: Please see the attached letter to Assistant Administrator Silva from the National Association of State Departments of Agriculture requesting a 30-day extension of the comment period in response to EPA's supplemental request for comments on perchlorate.

Attachment

September 18, 2009

The Honorable Peter S. Silva Assistant Administrator for Water U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, NW Washington, DC 20460

Re: Perchlorate Supplemental Request for Comments (Docket ID No. EPA-HQ- OW-2009-0297)

Dear Assistant Administrator Silva:

The National Association of State Departments of Agriculture (NASDA) respectfully requests a 30-day extension of the public comment period for the supplemental request for comments on perchlorate so that state regulators, as well as impacted sectors of our nation's agriculture economy, have an appropriate opportunity to review the approach EPA has taken in its evaluation of perchlorate.

NASDA represents the commissioners, secretaries, and directors of the state departments of agriculture in all fifty states and four U.S. territories. NASDA'S members are responsible for a wide range of public health programs from food safety to combating the spread of disease. Moreover, as co-regulators with EPA, NASDA's members are the lead state agencies responsible for administering, implementing and enforcing the laws regulating the production, labeling, distribution, sale, use and disposal of pesticides. This broad range of responsibilities gives our members a significant basis of relevant expertise in responding to the request for comment in the August 19, 2009 Federal Register.

We are concerned that the approaches EPA described in the August 19, 2009 Federal Register are a significant departure from the traditional methods by which EPA has analyzed scientific and technical data. Previous opportunities for public comment on the traditional approaches for analyzing data related to perchlorate have allowed for comments periods of up to 60 days. In light of this, and because the approaches detailed in the August 19, 2009 Federal Register differ significantly from those used for perchlorate and other Contaminant Candidates, an additional 30 days is necessary.

Response: See response to comment code 1600.

Commenter Name: Stephen Haterius
Commenter Organization: National Association of State Departments of Agriculture (NASDA)
EPA Document ID: EPA-HQ-OW-2009-0297-0664
EPA Comment ID: 28547
EPA Comment Code: 1600

Comment: October 8, 2009

Water Docket U.S. Environmental Protection Agency Mailcode: 2922T 1200 Pennsylvania Avenue, NW Washington, DC 20460

Re: Perchlorate Supplemental Request for Comments (Docket ID No. EPA-HQ-OW-2009-0297)

Dir Sir/Madam:

The National Association of State Departments of Agriculture (NASDA) represents the commissioners, secretaries, and directors of the state departments of agriculture in all fifty states and four U.S. territories. NASDA'S members are responsible for a wide range of public health programs from food safety to combating the spread of disease. Moreover, as co-regulators with the Environmental Protection Agency (EPA), NASDA's members are the lead state agencies responsible for administering, implementing and enforcing the laws regulating the production, labeling, distribution, sale, use and disposal of pesticides.

This broad range of responsibilities gives our members a significant basis of relevant expertise in responding to EPA's August 19, 2009 request for comment on alternative approaches to interpreting data related to EPA's earlier regulatory determination for perchlorate in drinking water. The comments NASDA is submitting today are intended to supplement comments submitted on September 18, 2009 in which NASDA requested additional time to review the approaches outlined by EPA.

Response: No response necessary to the information provided by the commenter.

EPA Comment Code: 2000 Perchlorate Health Effects

Response to Comment Code 2000: EPA used the January 2005 National Research Council (NRC) study "Health Implications of Perchlorate Ingestion," a review of the state of the science regarding potential adverse health effects of perchlorate exposure and mode of action for perchlorate toxicity (NRC, 2005) in developing this regulatory determination. The NRC recommended that EPA use data from the Greer *et al.* (2002) human clinical study as the basis for deriving a reference dose for perchlorate (NRC, 2005). Although the NRC committee concluded that hypothyroidism is the first adverse effect in the continuum of effects of perchlorate exposure, NRC recommended that "the most health-protective and scientifically valid approach" was to base the perchlorate RfD on the inhibition of iodide uptake by the thyroid, which the NRC considered a non-adverse effect (NRC, 2005). The NRC recommended that EPA apply an intraspecies uncertainty factor of 10 to the no observed effect level (NOEL)[1], to account for differences in sensitivity between the healthy adults in the Greer *et al.,* (2002) study and the most sensitive population, fetuses of pregnant women who might have hypothyroidism or iodide deficiency. They viewed this as conservative and protective of health given that the NOEL is based on a non-adverse effect (iodide uptake inhibition), which precedes the adverse effect in a continuum of possible effects of perchlorate exposure. The NRC also noted that "any decrease (in thyroid hormone) is potentially more likely to have adverse effects in sensitive populations (people with thyroid disorders, pregnant women, fetuses, and infants). EPA's Integrated Risk Information System (IRIS) adopted the NRC's recommendations resulting in an RfD of 0.7 µg/kg/day (USEPA, 2005b).

Individual Comments

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0469
EPA Comment ID: 19898
EPA Comment Code: 2000

Comment: I think you should regulate perchlorate in drinking water unless you know the following:

1. That perchlorate and thiocyanate don't have a synergistic effect within the thyroid by virtue of perchlorate inhibiting the conversion of thiocyanate to sulfate within the thyroid. Such an effect would increase the level of toxic sulfite in the thyroid. EPA chemist Ed Urbanski told me the EPA considered molybdenum co-factor enzymes, and perhaps subunits of those enzymes (sulfite oxidase is a subunit of nitrate reductase) to be perchlorate targets.

2. That adhesion of perchlorate to albumin and similar proteins in the blood and skin, which occurs in the blood before inhibition of the sodium iodide symporter and continues in the skin after perchlorate is cleared from the blood and thyroid, never forms a hapten that triggers an autoimmune reaction similar to iododerma and bromoderma. This seemed pertinent to Burleson's skin contact

[1] No observed effect level (NOEL) - an exposure level at which there are no statistically or biologically significant increases in the frequency or severity of any effect between the exposed population and its appropriate control.

sensitivity data in the 2002 external peer review, but there was no discussion of these traits of chaotropic salts in the EPA evaluation.

3. That perchlorate doesn't inhibit the effectiveness of defensin at its positively-charged 6-cysteine structure. Such an effect may help explain the aplastic anemia reported from medicinal doses of perchlorate by promoting infection by B-19 parvovirus. B-19 parvovirus is also associated with thyroid autoimmunity and thyroid cancer.

4. That pendrin is not the primary means of excreting perchlorate from the kidneys. If pendrin is the primary means of excreting perchlorate, then persons in a state of acidosis or low blood bicarbonate would retain perchlorate and be more vulnerable to its effects. Premature infants, infants with diarrhea, smokers, and adults with poorly managed diabetes in particular fit in this category of patient.

5. That extra-thyroidal sodium iodide symporter in the salivary glands, bronchial epithelium, gastric mucosa,and elsewhere in the body is not more sensitive to perchlorate than thyroidal sodium iodide symporter in the thyroid that is upregulated by TSH. Interference with proper function of non-thyroidal NIS may promote increased nitrosation in the gastric fluid, insufficient thiocyanate supply for myeloperoxidase, and gastrin imbalance. The function of NIS in the gastrointestinal tract was totally ignored in the EPA's decision not to regulate -- not a single GI tract specialist was consulted.

Response: EPA agrees with the commenter that the Agency should regulate perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard. EPA has considered and discusses in this Federal Register notice the results of current scientific literature on potential adverse biological effects, in the process of evaluating the adverse human health effects of perchlorate. The Agency analyzed the additional information, and EPA has determined that a national primary drinking water regulation for perchlorate would present a meaningful opportunity for health risk reduction for persons served by public water systems.

Commenter Name: M. Peterson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0937
EPA Comment ID: 20148
EPA Comment Code: 2000

Comment: Please review your decision regarding perchlorate regulation in water. The extremely high oxidizing potential of perchlorates produces radical species in water which have been determined as causing health problems - hydroxyl radicals, oxychlorides and the potential to form tri- and bi- halomethanes. The harsh effects of even low concentrations of highly oxidizing reactive species on organic tissues has not been fully studied and evaluated, yet their typical impacts have been determined to mutate and react to damage biological life forms.

Response: Please see the response to comment ID 19898 under comment code 2000.

Commenter Name: Gail Charnley
Commenter Organization: HealthRisk Strategies
EPA Document ID: EPA-HQ-OW-2008-0692-1073
EPA Comment ID: 20205
EPA Comment Code: 2000

Comment: RE: Docket ID No. EPA-HQ-OW-2008-0068 Comments on the US Environmental Protection Agency's Preliminary Regulatory Determination on Perchlorate November 5, 2008

Thank you for the opportunity to comment on the USEPA Office of Water's Preliminary Regulatory Determination on Perchlorate. My comments address the relative sensitivities of the mammary and thyroid glands to the iodine-uptake- inhibiting effects of perchlorate and the implications that difference has for perchlorate's reference dose (RfD). In short, scientific evidence indicates that the thyroid gland is 10 times more sensitive to the effects of perchlorate than the mammary gland; the 10X uncertainty factor currently incorporated into the RfD is thus protective not only of pregnant women but of nursing infants as well.

EPA's current RfD for perchlorate is, of course, based on perchlorate's ability to inhibit the thyroid gland's uptake of iodide by competing for the sodium (Na+)/iodide (I?) symporter (NIS), the protein responsible for transporting iodide into the thyroid gland for the purpose of synthesizing thyroid hormones. Because iodide uptake does not constitute an adverse effect itself, its choice as the basis for the RfD is health-protective. Insufficient iodide can result ultimately in changes in thyroid hormone levels, although normally such changes are compensated for. Insufficient thyroid hormone levels can impair normal fetal growth and development. Although studies have not specifically demonstrated adverse effects in children attributable to perchlorate,(1) the adverse effects of insufficient iodide are well known.

Because the perchlorate RfD was based on a study performed using healthy adults, it incorporates a 10X uncertainty factor to protect the most sensitive population the fetuses of pregnant women who might have hypothyroidism or iodide deficiency.(1) Iodide deficiency among pregnant women in the US is apparently not uncommon.(2)

Recent concern about the adequacy of perchlorate's RfD has focused on the results of studies demonstrating the presence of perchlorate in human milk at higher concentrations than in serum,(3) potentially posing a disproportionate risk to nursing infants. Although higher concentrations of milk perchlorate have not been associated with reduced milk iodide concentrations,(3) its presence in milk has led some to suggest that an additional uncertainty factor of 10 is needed to protect nursing infants.(4) An additional uncertainty factor of 10 is unnecessary, however, because the current RfD already protects nursing infants.

The current RfD protects nursing infants because the potency of perchlorate as an iodide uptake inhibitor has been shown to be ten times weaker for the mammary gland than for the thyroid gland.(5,6) In other words, it would take ten times as much perchlorate exposure to inhibit mammary iodide uptake to the same extent as thyroid iodide uptake. There are two possible explanations for the difference: the mammary NIS is simply different and less easily inhibited compared to the thyroid NIS, or there are two mechanisms by which the mammary gland takes up iodide and the non-NIS mechanism compensates in part for the NIS when the latter is inhibited.

There is no evidence supporting or refuting the first explanation but there is evidence supporting the second.(6)

The second mechanism by which the mammary gland obtains iodide is through the pendrin-iodide transporter.(7) When thyroid iodide uptake is inhibited, serum levels increase significantly, making more iodide available to the mammary gland (or placenta) and allowing the non-NIS mammary gland processes to help protect the newborn against inhibition.(8)

Thus because the mammary gland is ten times less sensitive to iodide uptake inhibition by perchlorate compared to the thyroid gland due to the presence of an iodide uptake mechanism that is not only unaffected by perchlorate but compensates for its effects, the current perchlorate RfD of 0.7 Âµg/kg/day is adequate to protect nursing newborns and an additional uncertainty factor is not needed.

I would be happy to provide further information upon request.

CITATIONS

(1) National Academy of Sciences/National Research Council (2005). Health Implications of Perchlorate Ingestion. National Academy Press. Washington, DC

(2) Caldwell KL, Jones R, Hollowell JG (2005). Urinary iodine concentration: United States. National Health And Nutrition Examination Survey 2001-2002.

Thyroid 15:692-699

(3) Pearce EN, Leung AM, Blount BC, Bazrafshan HR, He X, Pino S, Valentin- Blasini L, Braverman LE (2007). Breast milk iodine and perchlorate concentrations in lactating Boston-area women. Journal of Clinical Endocrinology and Metabolism 92:1673-1677; Kirk AB, Dyke JV, Martin CF, Dasgupta PK (2007). Temporal patterns in perchlorate, thiocyanate, and iodide excretion in human milk. Environmental Health Perspectives 115:182-186

(4) Ginsberg GL, Hattis DB, Zoeller RT, Rice DC (2007). Evaluation of the U.S. EPA/OSWER Preliminary Remediation Goal (PRG) for perchlorate in groundwater: Focus on exposure to nursing infants. Environmental Health Perspectives 115:361-369

(5) Tonacchera M, Pinchera A, Dimida A, Ferrarini E, Agretti P, Vitti P, Santini F, Crump K, Gibbs J (2004). Relative potencies and additivity of perchlorate,thiocyanate, nitrate, and iodide on the inhibition of radioactive iodide uptake by the human sodium iodide symporter. Thyroid 14:1012-1019; De Groef B, Decallonne BR, Van der Geyten S, Darras VM, Bouillon R (2006). Perchlorate versus other environmental sodium/iodide symporter inhibitors: potential thyroid-related health effects. European Journal of Endocrinology 155:17-25

(6) Potter GD, Tong W, Chaikoff IL (1959). The metabolism of 131I-labeled iodine, thyroxine, and triiodothyronine in the mammary gland of the lactating rat. Journal of Biological Chemistry 234:350-355; Dasgupta PK, Kirk AB, Dyke JV, Ohira S-I (2008). Intake of iodine and perchlorate and excretion in human milk. Environmental Science & Technology 42:8115-8121

(7) Rillema JA, Hill MA (2003). Prolactin regulation of the pendrin-iodide transporter in the mammary gland. American Journal of Physiology, Endocrinology, & Metabolism 284:E25-E28

(8) Clewell RA, Merrill EA, Gearhart JM, Robinson PJ, Sterner TR, Mattie DR, Clewell HJ (2007). Perchlorate and radioiodide kinetics across life stages in the human: Using PBPK models to predict dosimetry and thyroid inhibition and sensitive subpopulations based on developmental stage. Journal of Toxicology and Environmental Health, Part A 70:408-428

Response: EPA believes that the current RfD is protective of nursing infants and no uncertainty factor is necessary. Also, see response to comment code 2000.

Commenter Name: Caroline Baier-Anderson, PhD
Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20943
EPA Comment Code: 2000

Comment: Perchlorate Poses a Significant Risk to Human Health

The principle mode of action of perchlorate has been well-characterized: perchlorate blocks iodide uptake in the thyroid by the sodium (Na+)-iodide (I-) symporter (NIS), an ion channel initially identified as the mechanisms of iodide uptake in the basal membrane of thyroid follicular cells (Stanbury and Wyngaarden 1952; Wyngaarden et al. 1952), which is necessary for thyroid hormone synthesis. The selectivity of perchlorate for the sodium-iodide symporter (NIS) is as much as 30-fold greater than for iodide (Tonacchera et al. 2004) suggesting that low concentrations of perchlorate can out-compete iodide for uptake into the thyroid.

Significant inhibition of iodide uptake results in decreased production of iodine-rich thyroid hormones triiodothyronine (T3) and thyroxine (T4). Thyroid hormone production is regulated by a negative feedback system referred to as the hypothalamic-pituitary-thyroid axis. The thyroid produces T4 and T3; the pituitary gland produces thyroid stimulating hormone (TSH); and the hypothalamus produces thyrotrophic-releasing hormone (TRH). Cells in both the hypothalamus and pituitary gland respond to low levels of circulating T4 and T3; the hypothalamus stimulates the pituitary gland through TRH to produce TSH, which then prompts the thyroid to produce T4 and T3. Circulating plasma proteins can bind T4 and T3, serving as a reservoir. When thyroid production levels are low the output of TRH and TSH increase.

Response: EPA agrees that perchlorate may pose an adverse risk to human health, as discussed in more detail in the preamble announcing the final determination. Also, see response to comment code 2000.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-2082
EPA Comment ID: 21017
EPA Comment Code: 2000

Comment: P.O. Box 13222 Sacramento, CA95813 December 12, 2008

Dr. Melanie Marty, Chair Children's Health Protection Advisory Committee Air Toxicology and Epidemiology Branch Office of Environmental Health Hazard Assessment 1515 Clay Street Suite 1600 Oakland, CA 94612

Dr. Marty:

On behalf of the Perchlorate Study Group (PSG) I am writing in response to your November 3 letter to US EPA Administrator Steven Johnson regarding the Agency's preliminary determination on perchlorate. To be more specific, I'm writing in the hopes of addressing the various concerns you have raised and providing some additional perspective for your consideration.

First, a little about the PSG. As manufacturers and users of perchlorate, the PSG is committed to ensuring the best available science is provided in public debate and applied in the subsequent setting of regulatory standards. The member companies of the PSG include Aerojet, American Pacific (AMPAC), Alliant Techsystems (ATK), and Tronox.

By providing funding for scientific studies without interposition on the design, execution, or results for more than ten years, the PSG has worked cooperatively and effectively with the US Environmental Protection Agency (EPA) and other federal agencies, state governments, and water purveyors to:

* increase scientific and medical understanding of perchlorate's possible effects on human health; and,

* assess the level of perchlorate in drinking water that is not expected to cause adverse effects even in the most sensitive population.

We read your November 3 letter with great interest. In that letter, you raised several concerns with the scientific foundation of EPA's preliminary determination and questioned whether EPA gave sufficient consideration to the health effects of perchlorate on sensitive populations other than pregnant women and their fetuses.

As you are aware, EPA has been studying the health effects of perchlorate for more than 15 years releasing their first guidance document in 1992. Few chemicals have been the subject of such extensive research and so many peer- reviewed published studies. One of the unique scientific aspects of perchlorate is that we have a comprehensive understanding of how it affects the body. Due to its previous medical use and knowledge of the mechanism of action reduces uncertainty compared to most environmental chemicals. After several studies, draft risk assessments, guidance document revisions-- as well as an extensive and comprehensive review by the National Academy of Sciences (NAS), Agency for Toxic Substances and Disease Registry (ATSDR), and subsequent studies which have confirmed the NAS perchlorate panel's conclusions-- EPA is well positioned to issue its determination.

Response: EPA agrees that it has considered all relevant and best available science in making the final determination to regulate perchlorate. Also, see response to comment code 2000.

Commenter Name: Michael Girard

Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-2082
EPA Comment ID: 21019
EPA Comment Code: 2000

Comment: 2. Your letter asserts that EPA's decision does not take into account that the developing brain is sensitive to small decreases in thyroid hormone levels and that neonates have diminished stores of thyroid hormone relative to adults.

No references to support your position are provided in your letter. Thus it is difficult to assess the literature you may have used to support your statement. Nevertheless, there are some points to consider. First, thyroid hormones and pituitary hormones have normal and common temporal variability for a number of reasons (i.e., circadian rhythms, ambient temperature, etc.) Small changes in thyroid hormones are unlikely to cause long-term effects. To be adverse, changes due to chemical agents would have to be of a sustained, clinically significant magnitude over a period of time.

Second, a very small number of scientists have argued that the infant has less storage of iodine or thyroid hormone than the adult which would make the infant more vulnerable than the pregnant woman or its fetus. However, the RfD is based on no inhibition of iodide uptake, a non adverse and fully reversible effect. The half-life of perchlorate is short (approximately 8 hours) and it does not bioaccumulate. Basing an RfD that cautiously prevents the first step in the biochemical pathway would prevent any downstream event from occurring. Thus any differences between adults and children are not likely to be a factor since the first step, inhibition of IUI, is prevented. Moreover, in its assessment of perchlorate and the identification of the most sensitive population, the NAS considered all the relevant literature, including those reporting the storage and half life of thyroidal parameters. With their review, the NAS made the assessment that in pregnant women, infants and children, and people who have a low iodide intake or pre-existing thyroid dysfunction, the dose required to cause a decrease in thyroid hormone production may be lower. However, a dose that does not inhibit thyroid iodide uptake will not affect thyroid function, even in subjects with an abnormal thyroid gland or a very low iodide intake. (NAS, 2005)

Response: EPA has considered the sensitive subpopulations of newborns and infants. Please see the response to comment ID 21063 under comment code 4220 and response to comment ID 19898 under comment code 2000.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21055
EPA Comment Code: 2000

Comment: The EPA's National Center for Environmental Assessment (NCEA) prepared draft risk assessments for perchlorate in 1998 and 2002. The proposed reference doses (RfD) were 0.0009 mg/kg-day in 1998 and 0.00003 mg/kg-day in 2002. Using EPA's conventional (or default) conversion factors, these reference doses translated to drinking water values of 32 and 1 ppb, respectively. Both reference doses proposed by EPA/NCEA were based on the results of animal studies. In 2002, EPA/NCEA interpreted these studies as showing adverse effects in the pups of rats exposed during pregnancy to a perchlorate dose as low as 0.01 mg/kg-day (U.S. EPA, 2002).

Public comments on the 2002 draft risk assessment raised serious concerns about the validity of using these animal studies for human health risk assessment (U.S. EPA, 2003). The EPA, NRCA, and the Departments of Energy and Defense jointly sponsored a review of the underlying science by the NRC.

Response: EPA's determination to regulate perchlorate is based upon the National Research Council's 2005 (NRC, 2005) recommendation to use data from a human clinical study (Greer et al. 2002) as a basis for the human health risk assessment, and as a basis for the current RfD. On August 19, 2009, EPA published a FR Notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (FR Vol. 74, No. 159, p. 41883). In this August 19, 2009 FR Notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard. EPA has considered and discusses in the FR Notice the human health effects of perchlorate. The Agency analyzed the additional information received, and EPA has determined that perchlorate meets the criteria for regulating a contaminant in drinking water under Section 1412(b)(1)(A) of SDWA. See comment code 5000, 5100, 5200 and 5300 for further discussion of the criteria for a regulatory determination and EPA's decision to regulate perchlorate. Greer MA, Goodman G, Pleus RC, Greer SE. Health effects assessment for environmental perchlorate contamination: the dose response for inhibition of thyroidal radioiodine uptake in humans. Environ Health Perspect. 2002 Sep;110(9):927-37. Erratum in: Environ Health Perspect. 2005 Nov;113(11):A732. National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276 p.

Commenter Name: Kathy Curtis
Commenter Organization: Alliance of Nurses for Healthy Environments (ANHE)
EPA Document ID: EPA-HQ-OW-2009-0297-0651
EPA Comment ID: 28542
EPA Comment Code: 2000

Comment: A 1 ppb or lower MCL is supported by the most recent comprehensive studies, and these should be central to EPA's analysis. The industry-supported Greer study, which serves as the basis for EPA's current reference dose consisted of a 14-day study of 37 healthy adults. In more recent years, Blount et al analyzed a nationally representative sample of 2299 U.S. residents, and they have documented anti-thyroid effects in a large population of women exposed to perchlorate at concentrations far lower than levels previously shown to have such effects. This study and subsequent data clearly justify promulgation of a more protective MCL.

Response: On October 10, 2008, EPA published a FR Notice requesting public comments on its preliminary determination not to regulate perchlorate in drinking water (FR Vol. 73, No. 198, p. 60266). EPA has considered and discusses in the FR Notice the results of the Greer et al. (2002), and Blount et al. (2006) studies, in the process of evaluating the adverse health effects of perchlorate. The Blount et al. (2006) study investigated adverse effects of perchlorate exposure with women with urinary iodine below 100 ug/L, and revealed adverse thyroid hormone effects in women whose urinary iodine was below 100 ug/L, which is suggestive of a partial study population iodine deficiency status. EPA published additional analyses of these and other studies in August 2009. In this final determination, EPA evaluated the best available peer-reviewed science, and the

Agency has determined to regulate perchlorate in drinking water. An appropriate level for regulation has not yet been determined.

Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environ Health Perspect. 2006 Dec;114(12):1865-71.

Greer MA, Goodman G, Pleus RC, Greer SE. Health effects assessment for environmental perchlorate contamination: the dose response for inhibition of thyroidal radioiodine uptake in humans. Environ Health Perspect. 2002 Sep;110(9):927-37. Erratum in: Environ Health Perspect. 2005 Nov;113(11):A732.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28877
EPA Comment Code: 2000

Comment: In the Notice EPA describes alternative interpretations of health and exposure data for perchlorate that may impact EPA's final regulatory determination for perchlorate. EPA seeks comments on these alternatives in three areas:

* interpretation of physiologically-based pharmacokinetic (PBPK) modeling;

* derivation of alternative health reference levels (HRLs) based on body weight and water consumption rates for sensitive life stages; and

* use of data on perchlorate occurrence in drinking water.

To provide context for these comments, several points regarding the availability of scientific data on perchlorate are important. First, substantial research and evaluation of the potential health effects of perchlorate have been conducted. The scientific literature represents more than five decades of scientific inquiry. Since EPA began evaluating perchlorate in the early 1990s, scientists from government, industry, and academia have made important contributions to reducing uncertainties about the risks of perchlorate to public health (see footnote 4). In response to EPA's request for comment on its preliminary determination, Intertox reviewed the existing data (Intertox, 2008).[FN4: These comments were in response to the EPA FR notice Drinking Water: Preliminary Regulatory Determination on Perchlorate (U.S. EPA, 2008a).] Briefly, these data include:

* the 2005 NRC assessment of perchlorate and update of key studies that have been added to the scientific literature;

* at least twelve animal toxicological studies conducted between 1997 and 2002, all using EPA protocols, including pharmacokinetic, subchronic, developmental, and immunotoxicology studies, and a multigenerational reproductive study, conducted using a range of doses, and evaluated independently by EPA;

* several clinical and occupational exposure studies in humans and a number of epidemiologic and ecological studies between 1997 and 2002, some in occupational settings and some in populations exposed to perchlorate via the community drinking-water supply; and

* additional studies conducted since 2002, adding to the scientific literature.

Other agencies, e.g., the ATSDR (2008), have also conducted rigorous reviews of the scientific literature regarding the potential for adverse health effects from perchlorate exposure and have determined that doses equivalent to the current RfD are health protective.

Second, a no observed effect level (NOEL) has been identified for perchlorate exposure in humans. At the lowest dose of Greer et al. (2002) (the basis of the perchlorate RfD), there was no statistical difference in iodide uptake inhibition (IUI), a nonadverse effect, for subjects before and after a dose of 0.007 mg/kg-d (245 ppb assuming default body weight and drinking water intake).[FN5: The actual variable measured in Greer et al. (2002) was radioactive iodide uptake or RAIU.] As the NRC (2005) states with emphasis, "Inhibition of iodide uptake by the thyroid clearly is not an adverse effect; however if it does not occur, there is no progression to adverse health effects." Use of a NOEL is more conservative than EPA's common approach using the no observable adverse effect level (NOAEL) or the lowest observable adverse effect level (LOAEL).

Third, perchlorate is water soluble, has a half life in humans of approximately eight hours, and does not bioaccumulate. Because perchlorate has a short half life, some have questioned whether exposure to perchlorate might cause an acute effect. Toxicologically speaking, "acute" describes effects seen after one high dose or an exposure of less than 24 hours. No published study has demonstrated an effect after one exposure to perchlorate at environmental levels. The dose required for acute effects would require therapeutic levels; the medical literature reports that doses from 200 mg to over 1 gram given on a daily basis (the equivalent of 100,000 to 500,000 ppb in drinking water using standard EPA default assumptions[FN6: 1g = 1,000 mg; Drinking Water Equivalent for 1,000 mg perchlorate / 2 L of water per day = 500 mg/L or 500 ppm or 500,000 ppb; Drinking Water Equivalent for 200 mg would be 100 ppm or 100,000 ppb.]) are necessary to cause side effects (e.g., nausea and gastrointestinal upset at lower doses to aplastic anemia and agranulocytosis at daily doses of one gram or more) in 5 to 18 percent of study populations (NRC, 2005; Barzilai and Sheinfeld, 1966). At exposures lasting several weeks to months (more commonly termed "subchronic"), the scientific literature does not demonstrate any evidence of adverse effect. Thyroxine (T4) has a half life of 6-8 days and must be sufficiently depleted for developmental effects to occur. A single perchlorate dose in excess of 1 gram per day would most likely cause some frank toxicity, but based on the science to date, will not decrease serum thyroid hormone levels without daily exposure for weeks.

Fourth, the NRC's recommendation to base the RfD on a NOEL was conservative and health protective, as this dose is lower than any dose at which adverse effects may occur. To derive the RfD, the NOEL was divided by an uncertainty factor (UF) of 10 to account for the most sensitive individuals in a population, the hypothyroid or iodine-deficient pregnant women and their developing fetuses. The NRC committee stated that using a NOEL as the point of departure (POD) is a more conservative and health protective approach than EPA's customary approach of using the adverse effect (NRC, 2005). For example, the use of the threshold for IUI as a POD is more conservative and health protective than using changes in thyroid hormones (also a precursor to possible adverse effects) or an adverse effect such as hypothyroidism.

Perchlorate's reversible inhibition of the NIS is documented in many experiments, both in vivo and in vitro. This interaction exhibits the standard sigmoidal dose-response curve in toxicology and pharmacology-as dose increases, so does the response. There is no scientific evidence to suggest that low doses of perchlorate will cause any other effect. Perchlorate competitively inhibits iodide uptake; it neither mimics a hormone nor directly stimulates a response.

Response: See response to comment code 2000.

EPA Comment Code: 2100 NAS (NRC) review of perchlorate health effects and reference dose

Response to Comment Code 2100: On October 10, 2008, EPA published a Federal Register notice presenting the Agency's preliminary regulatory determination for perchlorate and supporting rational for this determination, in accordance with the Safe Drinking Water Act (SDWA) (Federal Register Vol. 73, No. 198, p. 60262). In this October 10, 2008 Federal Register notice, EPA determined that a national primary drinking water regulation (NPDWR) for perchlorate would not present a meaningful opportunity for health risk reduction for persons served by public water systems. In 2003, the National Research Council (NRC) of the National Academy of Sciences (NAS) was asked by EPA to assess the current state of the sciences regarding potential adverse effects of perchlorate exposure in human and animals, and to determine whether EPA's prior perchlorate risk assessment findings were consistent with current scientific evidence. In a NRC 2005 review of the state of the sciences regarding potential perchlorate adverse health effects and mode-of-action ("Health Implications of Perchlorate Ingestion", NRC 2005), the NRC recommended that data from the Greer et al. (2002) human clinical study be used as the basis for deriving a perchlorate reference dose (RfD)(NRC 2005). From this Greer et al. (2002) human clinical study, the statistical no observed effect level (NOEL) for the perchlorate-induced inhibition of thyroid iodide uptake was determined to be 7.0 ug/kg, which corresponded to an iodide uptake inhibition of 1.8 %. The NRC concluded that the most health protective and scientifically valid approach to deriving a reference dose for perchlorate was to base the perchlorate RfD on the inhibition of iodide uptake by the thyroid, and that iodide uptake inhibition, though not an adverse effect per se, is the most appropriate precursor event, and would precede any more severe adverse health effects of perchlorate exposure in humans. The NRC recommended basing the RfD on a precursor to an adverse effect rather than an adverse effect per se. The precursor event precedes a downstream adverse effect in the dose response continuum. In this case, NRC used prevention of iodide uptake inhibition, a precursor to adverse thyroid effects, to establish a level at which no adverse effects would be anticipated in exposed populations. This approach is consistent with the Agency's policy on the use of precursor events when appropriate in establishing the critical effect upon which an RfD is based (U.S. EPA, 2002). The NRC recommended that EPA apply an uncertainty factor of 10 to this NOEL of 7.0 ug/kg for the perchlorate-induced inhibition of thyroid iodide uptake, to account for differences in sensitivity between healthy adults and the most sensitive sub-population, consisting of fetuses of pregnant women who might have hypothyroidism or iodide deficiency. The NRC viewed the recommended uncertainty factor of 10 as conservative and protective of health, given that the NOEL is based on a non-adverse effect (iodide uptake inhibition) which precedes the adverse effect in a continuum of possible adverse biological effects of perchlorate exposure. NRC recommended that using a non-adverse effect that is upstream of the adverse effect represents a more conservative, health-protective approach to the risk assessment for perchlorate, noting that the purpose of the 10-fold uncertainty factor is to protect sensitive subpopulations in the face of uncertainty regarding their relative sensitivity to perchlorate exposure. EPA has adopted the NRC's recommendations in its "Integrated Risk Information System" (IRIS) (USEPA 2005), resulting in an RfD of 0.7 ug/kg/day, which was derived by applying a 10-fold (10x) uncertainty factor to the NOEL of 7.0 ug/kg/day.

EPA believes the NRC appropriately based the RfD on iodide uptake inhibition to the thyroid, for the reasons discussed in its report. EPA notes that the data underlying the definition of iodide uptake inhibition as a precursor effect and the relationship of iodide uptake inhibition to the

continuum of adverse outcomes reflects an understanding of effects in adults; it may not reflect the relationship of the precursor event to adverse outcomes in neonates and infants, who may not have iodide stores sufficient to offset the effects of reduced iodide uptake. The less resilient neonatal and infant system makes the exposure gap between a precursor event (iodide uptake inhibition due to perchlorate) and reduced T3/T4 levels likely to be narrower than for adults, and in fact, the distinction between the two may be blurred for the very young (Greer et al., 2002; Savin et al., 2003; van den Hove et al., 1999). The NRC noted that, "[T]he minimal prolonged decrease in thyroid hormone production that would be associated with adverse health effects is not known; any decrease is potentially more likely to have adverse effects in sensitive populations (people with thyroid disorders, pregnant women, fetuses, and infants) but data are not available to determine the magnitude of the decrease needed to cause adverse effects in those populations."

Individual Comments

Commenter Name: Melanie A. Marty, Ph.D.
Commenter Organization: Children's Health Protection Advisory Committee
EPA Document ID: EPA-HQ-OW-2008-0692-0962
EPA Comment ID: 20418
EPA Comment Code: 2100

Comment: We note that the RfD itself is uncertain and is not necessarily a health protective benchmark. It is based upon a limited clinical study of short duration and small sample size not representative of the variability in the human population (Greer, et al., 2002). When a larger epidemiologic study was conducted by CDC, significant correlations were found between increasing perchlorate exposure and decreasing thyroid hormone levels in the subpopulation of women with low iodide intake, which the CDC NHANES data show constitutes 31% of all women (Blount, et al 2006). The exposure levels associated with anti- thyroid effects in these women were below the perchlorate RfD. These findings cast doubt on the protectiveness of the RfD, and make it especially important that no group exceed this health benchmark.

Response: See response to comment ID 28936 under comment code 2100.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association
EPA Document ID: EPA-HQ-OW-2008-0692-1424
EPA Comment ID: 20439
EPA Comment Code: 2100

Comment: Exposure

In addition to occurrence, the evaluation criteria in the SDWA also consider whether contamination is occurring at levels "of public health" concern and whether regulation of the contaminant would meaningfully reduce potential health risks. AWWA would like to acknowledge and compliment the National Research Council for the extensive assessment of risk that resulted in setting the oral Reference Dose (RfD) at 7x10-4 mg/kg-day. In consideration of the SDWA criteria, it should be emphasized that the RfD represents a No Observed Effect Level (NOEL) versus the more traditional No ObservedAdverse Effect Level (NOAEL). As discussed by Crawford-Brown et.al.

(2006) and in the proposed decision, a NOAEL is by definition equal to or higher than a NOEL wherethe effect used to establish the NOEL is a precursor to the adverse effect of interest in establishing a NOAEL. The NRC's use of a precursor to an adverse effect (iodine uptake inhibition) in establishing a threshold for exposure represents a "more conservative, health-protective approach". This assures the protection of the sensitive subpopulation (iodide-deficient pregnant women and their fetuses) and mitigates the need for additional uncertainty factors to be applied.

Response: EPA does not agree that use of precursor effect alters the need for uncertainty factors. Uncertainty factors are applied to respond to specific aspects of uncertainty in some aspect of the health assessment, regardless of the nature of the endpoint used. Examples include intraspecies or interspecies variability, data gaps, or discrepancies in time course of the study compared to the anticipated effect/exposure profile in the public. Also, see response to comment code 2100.

Commenter Name: Gregg Grunenfelder
Commenter Organization: Washington State Department of Health; and Oregon Department of Human Services
EPA Document ID: EPA-HQ-OW-2008-0692-1529
EPA Comment ID: 20454
EPA Comment Code: 2100

Comment: Perchlorate interferes with iodide uptake and affects the release of thyroid hormones. Appropriate levels of thyroid hormones are critical to the development of the brain and other organs, making the fetus and newborn infant particularly sensitive to perchlorate toxicity. Maternal exposure to elevated levels of perchlorate has been linked to mild, in some cases severe and irreversible, neurological outcomes in infants. Perchlorate is but one more contaminant along with mercury, PCBs, PBDEs, and lead that adversely impact the developing brain.

Washington Department of Health and Oregon Department of Human Services, Public Health Division believe that the 10-fold uncertainty factor used by EPA to derive a Reference Dose (RfD), and its subsequent use to formulate a health based drinking water level, is insufficient.

We believe that due to the data gaps in the limited studies available for perchlorate that a higher uncertainty factor is warranted. Back in 2002, EPA more appropriately utilized a higher uncertainty factor in the agency's assessment of perchlorate, as did the state of Massachusetts in their in-depth risk assessment of perchlorate. Exposure estimates based on a more protective RfD indicate that, at any one time, as many as 210,000 pregnant women in the US are exposed to unsafe levels of perchlorate. This view of risk could well influence the conclusion as to whether or not a national regulation of percholorate in drinking water presents a meaningful opportunity to protect public health.

As state regulators, we strive to evaluate chemical hazards in a consistent manner. If EPA had used its standard risk assessment methodology, their findings of the hazards of perchlorate in drinking water would have been significantly different. We recommend that EPA reconsider its evaluation since there is no obvious scientific reason for using the different methodology which led to this preliminary determination.

We support the scientific approach reflected in the enclosed information prepared by the Washington Department of Health, and ask that EPA carefully consider it as your agency

determines the appropriate next step. Further, if we can provide any further information regarding this important public health issue, please contact us, Gregg Grunenfelder, Washington State Department of Health, (360.236.3050) or Gail Shibley, Oregon State Department of Human Health Services (971.673.0400).

Sincerely,

Gregg Grunenfelder, Assistant Secretary Washington State Department of Health Division of Environmental Health

Gail R. Shibley, Administrator Oregon State Department of Human Services Office of Environmental Public Health

Response: Please see response to comment ID 28818 under comment code 2100.

Commenter Name: Gregg Grunenfelder
Commenter Organization: Washington State Department of Health; and Oregon Department of Human Services
EPA Document ID: EPA-HQ-OW-2008-0692-1529
EPA Comment ID: 20455
EPA Comment Code: 2100

Comment: Enclosure

November 10, 2008 Docket ID No. EPA-HQ-OW-2008-0692 Comments on EPA's Preliminary Regulatory Determination for Perchlorate Prepared by Washington State Department of Health

On October 10, 2008, the US Environmental Protection Agency (EPA) placed an action notice on the Federal Register [FN1: EPA 2008. Fact Sheet: Preliminary Regulatory Determination for Perchlorate. Office of Water. United States Environmental Protection Agency. EPA 815-F-08-009. October 2008.],[FN2: Federal Register: October 10, 2008 (Volume 73, Number 198). Notices. Page 60262-60282. From the Federal Register Online via GPO Access [wais.access.gpo.gov] [DOCOD:fr10oc08-66].] relating to preliminary regulatory determination for perchlorate in accordance with the federal Safe Drinking Water Act. The agency determined that a national primary drinking water regulation for perchlorate would not present "a meaningful opportunity for health risk reduction for persons served by public water systems." EPA will make a final regulatory determination for perchlorate after considering public comments and information provided during the 30-day comment period ending November 10, 2008. EPA intends on publishing its final regulatory determination in December 2008 to provide state and local public health officials with technical information that can be used to address local contamination.

Perchlorate (ClO4) is a naturally occurring inorganic compound that can also be manufactured. Ammonium perchlorate (NH4ClO4), is a salt used as an oxidizer in rocket propellants and fireworks. It has also been found in certain fertilizers, and was used in the past as a medicine to treat hyperthyroidism (overactive thyroid) in humans. Perchlorate salts are ionic and dissociate completely when dissolved in water. The soluble anion ClO4 has been found in groundwater in many states where testing has occurred. To date, it is not clear to what extent perchlorate is found in groundwater across the United States, because it has not been widely studied. In the northwest, low

levels of perchlorate have been found in groundwater in some tested areas of eastern Washington and Oregon.

Perchlorate interferes with the thyroid's ability to take in iodide. The thyroid needs iodide to produce certain hormones that are necessary for numerous body functions. If the thyroid is unable to produce enough of these hormones, a condition known as hypothyroidism (underactive thyroid disease) may result. Thus, perchlorate exposure has the potential to result in hypothyroidism.

All people are susceptible to perchlorate's effects on the thyroid (decreased iodide uptake), but pregnant women, infants, children, and people with low iodide intake in the diet, or pre-existing thyroid problems may be more susceptible. Hypothyroidism, if untreated, can lead to numerous health effects including, fatigue, muscle aches, unexplained weight-gain, depression, and many other symptoms. Moreover, hypothyroidism in pregnant women (developing fetuses), infants, and children can lead to impaired mental and physical development. Maternal exposure to elevated levels of perchlorate has been linked to mild, and in some cases severe and irreversible neurological outcomes in infants. Similar adverse outcomes to the developing fetus have been documented with exposure to mercury, PCBs, PBDEs, and lead.

In the absence of federal regulatory standards on perchlorate, several states have developed Reference Doses (RfD) or safe doses that are used to derive safe drinking water guidance or standards. Most notably are recent efforts by EPA [FN3: EPA 2002. Perchlorate environmental contamination: toxicological review and risk characterization. External Review Draft. United States Environmental Protection Agency. Office of Research and Development. NCEA-1-0503. January 16, 2002.], California [FN4: Ting D, Howd RA, Fan AM, and Alexeeff GV. 2006. Development of a Health-Protective Drinking Water Level for Perchlorate. Environmental Health Perspectives (114)6: 881-86.],[FN5: California Environmental Protection Agency. 2004. Office of Environmental Health Hazard Assessement. Public Health Goals for Chemicals in Drinking Water: Perchlorate. March 2004.], New Jersey [FN6: New Jersey Department of Environmental Protection 2005. New Jersey Drinking Water Quality Institute. Maximum Contaminant Level Recommendation for Perchlorate. October 7, 2005.], Massachusetts [FN7: Massachusetts Department of Environmental Protection. 2006. Office of Research and Standards. Update to "Perchlorate Toxicological Profile and Health Assessment". March 2006.], and the National Research Council of the National Academy of Science (NAS) [FN8: National Academy of Sciences. 2005. Health Implication of Perchlorate Ingestion. National Academies Press. Washington D.C. Available at URL: http://www.nap.edu/catalog.php?record_id=11202].

EPA conducted the initial draft toxicological review of perchlorate in 2002, resulting in a proposed RfD of 0.00003 mg/kg/day based primarily on studies that identified neurodevelopmental deficits in rat pups [FN9: Argus 2001. Hormone, thyroid, and neurohistological effects of oral (drinking water) exposure to ammonium perchlorate in pregnant and lactating rats and in fetuses and nursing pups exposed to ammonium perchlorate during gestation or via maternal milk. Argus Research Laboratories, Inc. Horsham, PA. Protocol no. ARGUS 1416-003. Cited in EPA 2002.]. These deficits were linked to maternal exposure to perchlorate. Subsequent to this assessment, California, New Jersey, the NAS, and Massachusetts reviewed the health implications of perchlorate, and each proposed an alternative reference dose of 0.0004, 0.0007, 0.0007, and 0.00003 mg/kg/day, respectively. This is based primarily on a study on humans conducted by Greer et al. published in 2002. A summary of perchlorate reference doses developed by the various agencies is presented in Table 1.

[Table 1. Comparison of Perchlorate Reference Doses (RfD) Developed by Other Agencies - see PDF Docket ID EPA-HQ-OW-2008-0692-1259]

In the Greer et al. [FN10: Greer MA, Goodman, F, Pleus RC, and Greer SE. 2002. Health Effects Assessment for Environmental Perchlorate Contamination: The Dose Response for Inhibition for Thyroid Radioiodine Uptake in Humans. Environmental Health Perspectives (110)9: 927-37.] study cited by four of the five agencies, 37 human subjects were split into four exposure groups and administered oral doses of perchlorate at 0.007 (7 subjects), 0.02 (10 subjects), 0.1 (10 subjects), and 0.5 (10 subjects) mg/kg/day. Significant decreases in iodide uptake were found in the three highest exposure groups. Iodide uptake was not significantly reduced in the lowest exposed group, but four of the seven subjects in this group experienced inhibited iodide uptake. The RfD proposed by NAS was accepted by EPA and added to its integrated risk information system (IRIS) in 2005.

Much debate was generated following EPA's posting of the RfD in IRIS, most notably in commentary submitted to the journal Environmental Health Perspectives by Ginsberg and Rice [FN11: Ginsberg G and Rice D. 2005. The NAS Perchlorate Review: Questions Remain about the Perchlorate RfD. Environmental Health Perspectives (115)3: 361-69.]. The authors argued that the RfD was not adequately protective of human health for the following reasons:

1. The NAS report described the level of lowest exposure from Greer et al. as a no observed effect level (NOEL). However, there was actually an effect at that level although not statistically significant largely due to small size of study population (four of seven subjects showed a slight decrease in iodide uptake).

2. Reduced iodide uptake was not considered an adverse effect. However, it is a precursor to an adverse effect (hypothyroidism). Therefore, additional safety factors are necessary when extrapolating from the point of departure to the RfD.

3. Consideration of data uncertainty was insufficient because the Greer, et al. study reflected only a 14-day exposure to healthy adults and no additional safety factors were considered to protect sensitive subpopulations. For example, the potential for greater toxicity to breastfeeding newborns was not considered.

Response: EPA believes that the RfD recommended by the NAS remains appropriate, as discussed in the other responses to comments in this section (comment code 2100); however, EPA will be continue to evaluate scientific studies of perchlorate health effects as the Agency develops the National Primary Drinking Water Regulation for perchlorate.

Commenter Name: Gregg Grunenfelder
Commenter Organization: Washington State Department of Health; and Oregon Department of Human Services
EPA Document ID: EPA-HQ-OW-2008-0692-1529
EPA Comment ID: 20458
EPA Comment Code: 2100

Comment: The Department of Health's Conclusions:

There is consensus among agencies that the Greer et al. study is appropriate for deriving the RfD, but there is not consensus with regard to developing drinking water maximum contaminant levels (MCLs) or action levels. One of the key differences results from how the point of departure is viewed [i.e., No observed effect level (NOEL) or lowest observed adverse effect level (LOAEL)], or whether a benchmark dose should be used to derive the RfD. Defining the point of departure as a NOEL or LOAEL has implications when it comes to applying appropriate safety factors to the point of departure to derive the RfD.

Based on a review of existing literature, the Department of Health has identified the following concerns with EPA's perchlorate action level:

* EPA's RfD, which is the basis for the health reference level, may not be protective of public health with a reasonable margin of safety.

Response: Please see response to comment code 2100 for a discussion of the RfD. See Response to comment code 5220 for a discussion of alternative Health Reference Levels. EPA will continue to refine its analyses for purposes of proposing an MCL and MCLG. EPA plans to seek comment on the proposed national drinking water regulation pursuant to the requirements of the Safe Drinking Water Act.

Commenter Name: Carol Bigelow
Commenter Organization: University of Massachusetts
EPA Document ID: EPA-HQ-OW-2008-0692-1427
EPA Comment ID: 20630
EPA Comment Code: 2100

Comment: We also found critical errors in the selection, design and interpretation of the studies that were included in docket ID No. EPA-HQ-OW-2008-0692. The irrelevant studies should be dropped from the docket, the flawed interpretations of the remaining studies should be corrected, and the conclusions drawn revised.

Several studies reported in docket ID No. EPA-HQ-OW-2008-0692 are either inappropriate for inclusion, or erred in their design or interpretation. Most significant in this regard is the population that was emphasized by the EPA in citing the NAS report of 2005 (NRC, 2005): pregnant adults. EPA provided no scientific justification for this emphasis. Moreover, the emphasis on the pregnant adult illustrates the mistake of public health recommendations by persons who are not at significant risk. As we've noted above: "the adult thyroid system appears capable of significant compensation for low thyroid hormone levels, and the consequences of low thyroid hormone are likely to be reversible."

Response: EPA respectfully disagrees with the commenter. It is also noted that the commenter does not specify which studies she is critical of. In a NRC 2005 review of the state of the sciences regarding potential perchlorate adverse health effects and mode-of-action ("Health Implications of Perchlorate Ingestion", NRC (2005)), the NRC recommended that data from the Greer et al. (2002) human clinical study be used as the basis for deriving a perchlorate reference dose (RfD) (NRC 2005). From this Greer et al. (2002) human clinical study, the statistical no observed effect level (NOEL) for the perchlorate-induced inhibition of thyroid iodide uptake was determined to be 7.0 ug/kg, which corresponded to an iodide uptake inhibition of 1.8%. The NRC concluded that the

most health protective and scientifically valid approach to deriving a reference dose for perchlorate was to base the perchlorate RfD on the inhibition of iodide uptake by the thyroid, and that iodide uptake inhibition, though not an adverse effect per se, is the most appropriate precursor event, and would precede any more severe adverse health effects of perchlorate exposure in humans. The NRC recommended basing the RfD on a precursor to an adverse effect rather than an adverse effect per se. The precursor event precedes a downstream adverse effect in the dose response continuum. In this case, NRC used prevention of iodide uptake inhibition, a precursor to adverse thyroid effects, to establish a level at which no adverse effects would be anticipated in exposed populations. This approach is consistent with the Agency's policy on the use of precursor events when appropriate in establishing the critical effect upon which an RfD is based (U.S. EPA, 2002). The NRC recommended that EPA apply an uncertainty factor of 10 to this NOEL of 7.0 ug/kg for the perchlorate-induced inhibition of thyroid iodide uptake, to account for differences in sensitivity between healthy adults and the most sensitive sub-population, consisting of fetuses of pregnant women who might have hypothyroidism or iodide deficiency. Iodide uptake inhibition has been identified in the literature as an area of concern in connection with increasing the risk of neurodevelopmental impairment in fetuses of high-risk mothers. The NRC viewed the recommended uncertainty factor of 10 as conservative and protective of health, given that the NOEL is based on a non-adverse effect (iodide uptake inhibition) which precedes the adverse effect in a continuum of possible adverse biological effects of perchlorate exposure. NRC recommended that using a non-adverse effect that is upstream of the adverse effect represents a more conservative, health-protective approach to the risk assessment for perchlorate, noting that the purpose of the 10-fold uncertainty factor is to protect sensitive subpopulations in the face of uncertainty regarding their relative sensitivity to perchlorate exposure. EPA has adopted the NRC's recommendations in its "Integrated Risk Information System" (IRIS) (USEPA, 2005), resulting in an RfD of 0.7 ug/kg/day, which was derived by applying a 10-fold (10x) uncertainty factor to the NOEL of 7.0 ug/kg/day. Greer MA, Goodman G, Pleus RC, Greer SE. Health effects assessment for environmental perchlorate contamination: the dose response for inhibition of thyroidal radioiodine uptake in humans. Environ Health Perspect. 2002 Sep;110(9):927-37. National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276pp. USEPA. 2002. A review of the reference dose and reference concentration processes. Risk Assessment Forum, Washington, DC; EPA/630/P–02/0002F. USEPA. 2005. "Integrated Risk Information System (IRIS), Perchlorate and Perchlorate Salts." February 2005.

Commenter Name: Michael Dourson
Commenter Organization: Toxicology Excellence for Risk Assessment
EPA Document ID: EPA-HQ-OW-2008-0692-1562
EPA Comment ID: 20641
EPA Comment Code: 2100

Comment: Our primary concern is related to the RfD EPA used to estimate Health Reference Level. Our comments follow three lines of evaluation:

1. Critically important data on pregnant women and their offspring have become available since the time of the development of the EPA RfD in 2005 (EPA, 2008), which necessitate a reconsideration of the existing value. This reconsideration is consistent with recommendations of the NAS (2005) on page 69 of its report.

2. The excellent relative source contribution evaluation of EPA, based on well supported and clearly described work of the FDA, necessitates a rethinking of the EPA's RfD, since the subjects in Greer et al. (2002) on which it was based undoubtedly had unmeasured perchlorate in their food.

3. The 2005 NAS "RfD" does not follow the existing EPA RfD method.

All three of these arguments are more fully discussed below. We also offer a commentary on the Blount et al. (2007) that may have some bearing on this federal action (Attachment A). Note, while a reanalysis of the RfD will not have an effect on the regulatory conclusion discussed in this Federal Register notice, it will have an effect on the Health Advisory that EPA derives, which will be used by States for their regulation of perchlorate.

Response: See response to comment ID 20957 under comment code 2100 for a discussion of adjusting the Greer study to account for perchlorate which may have been in subjects' food. EPA supports the review and evaluation of additional new data regarding the health effects of perchlorate. However EPA respectfully disagrees with the commenter regarding the NRC (2005) recommendations for the RfD, as discussed below. EPA will continue to evaluate scientific studies of perchlorate health effects as part of the perchlorate rulemaking

The EPA "Integrated Risk Information System" (IRIS) employs EPA's standard risk assessment methodology. The RfD, which is derived from the NOEL, is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population that is likely to be without an appreciable risk of deleterious effects during a lifetime. The RfD, based on the assumption that thresholds exist for certain toxic effects of chemicals, represents the drinking water perchlorate exposure plus an incremental additional exposure of perchlorate from either water or food which could trigger iodine uptake inhibition, with a 10X safety factor applied. The NRC recommended that data from the Greer et al. (2002) human clinical study be used as the basis for deriving a perchlorate reference dose (RfD) (NRC 2005), and also noted that the results of this study were supported by those of other human studies. From this Greer et al. (2002) human clinical study, the statistical no observed effect level (NOEL) for the perchlorate-induced inhibition of thyroid iodide uptake was determined to be 7.0 ug/kg (a corresponding iodide uptake inhibition of 1.8%). The NRC concluded that the most health protective and scientifically valid approach was to base the perchlorate RfD on the precursor event of inhibition of iodide uptake by the thyroid. This approach is consistent with the Agency's policy on the use of precursor events when appropriate in establishing the critical effect upon which an RfD is based (U.S. EPA, 2002). The NRC recommended that EPA apply an uncertainty factor of 10 to this NOEL of 7.0 ug/kg to account for differences in sensitivity between healthy adults and the most sensitive sub-population (fetuses of pregnant women who might have hypothyroidism or iodide deficiency). Iodide uptake inhibition due to perchlorate exposure has been identified as an area of concern in connection with increasing the risk of neurodevelopmental impairment in fetuses of high-risk mothers. The NRC viewed the recommended uncertainty factor of 10 as conservative and protective of health. NRC recommended that using a non-adverse effect that is upstream of the adverse effect represents a more conservative, health-protective approach to the risk assessment for perchlorate, noting that the purpose of the 10-fold uncertainty factor is to protect sensitive subpopulations in the face of uncertainty regarding their relative sensitivity to perchlorate exposure. EPA has adopted the NRC's recommendations in its "Integrated Risk Information System" (USEPA, 2005), resulting in an RfD of 0.7 ug/kg/day, which was derived by applying a 10-fold uncertainty factor to the NOEL of 7.0 ug/kg/day. EPA

used the best available peer-reviewed science, and the Agency has determined to regulate perchlorate in drinking water.

Greer MA, Goodman G, Pleus RC, Greer SE. Environ Health Perspect. 2002 Sep;110(9):927-37. National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276pp. USEPA. 2002. A review of the reference dose and reference concentration processes. Risk Assessment Forum, Washington, DC; EPA/630/P–02/0002F. USEPA. 2005. "Integrated Risk Information System (IRIS), Perchlorate and Perchlorate Salts." February 2005.

Commenter Name: Michael Dourson
Commenter Organization: Toxicology Excellence for Risk Assessment
EPA Document ID: EPA-HQ-OW-2008-0692-1562
EPA Comment ID: 20642
EPA Comment Code: 2100

Comment: Availability of New Data

Critically important data on pregnant women and their offspring have become available since the time of the development of the 2005 EPA's Reference Dose (RfD) (EPA, 2008), which necessitate a reconsideration of the existing value.

For example, although the NAS recommended that the Greer et al (2002) be used as the basis of the RfD, the NAS also recognized that new, useful data were under development:

"On the basis of the iodide-inhibition analyses, the additional comparisons, and a review of information on urinary iodide excretion, the committee concluded that the data from Chile could be considered in the evaluation of the U.S. experience with perchlorate in drinking water." (NAS, 2005, page 69)

The data to which NAS referred was published prior to the NAS report as Crump et al. (2000), and after the NAS report as Tellez et al. (2005), the abstract of which reads:

"We have conducted a longitudinal epidemiologic study among pregnant women from three cities in northern Chile: Taltal with 114 ug/L, Chañaral with 6 ug/L, and Antofagasta with 0.5 ug/L perchlorate in the public drinking water. We tested the hypothesis that long-term exposure to perchlorate at these levels may cause a situation analogous to iodine deficiency, thus causing increases in thyrotropin (TSH) and thyroglobulin (Tg) levels and decreased levels of free thyroxine (FT4), in either the mother during the early stages of gestation or the neonate at birth, or in the fetus cause growth retardation. We found no increases in Tg or TSH and no decreases in FT4 among either the women during early pregnancy (16.1 +/- 4.1 weeks), late pregnancy (32.4 +/- 3.0 weeks), or the neonates at birth related to perchlorate in drinking water. Neonatal birth weight, length, and head circumference were not different among the three cities and were consistent with current U.S. norms. Therefore, perchlorate in drinking water at 114 ug/L did not cause changes in neonatal thyroid function or fetal growth retardation. Median urinary iodine among the entire cohort was 269 ug/L, intermediate between that of pregnant women in the United States at National Health and Nutrition Examination Survey (NHANES) I and at NHANES III and consistent with current World Health Organization (WHO) recommendations. Median breast milk iodine was not decreased

in the cities with detectable perchlorate. Analysis of maternal urinary perchlorate excretion indicates an additional dietary source of perchlorate." (Tellez et al., 2005)

In addition, EPA has discussed other data relevant to deriving an updated RfD in this Federal Register notice, including Amitai et al., 2007, Blount et al., 2006b (see a separate discussion of Blount in Attachment A), and the studies discussing PBPK models (Merrill et al., 2005; Clewell et al., 2007).

Contribution of Perchlorate in Food to Total Exposure

As EPA discussed in this Federal Register notice, the US population is being exposed to perchlorate through both food and water. Based on EPA's excellent relative source contribution evaluation (Table 6), the dose of perchlorate from food could range from 0.075 ug/kg-day (median dose) to 0.167 ug/kg-day (90th percentile dose) and account for 24% of total perchlorate exposure for the general population.

This information may necessitate a rethinking of the 2005 RfD based on Greer et al. (2002). Since these investigators did not measure perchlorate in the food of the human subjects, it is likely the total perchlorate dose received by the subjects was higher than the drinking water dose of 0.007 mg/kg-day that was used as the point of departure for the RfD. This same consideration might also be appropriate for RfDs based on other human studies.

The 2005 NAS "RfD" does not follow the existing EPA RfD method.

While we agree that perchlorate causes adverse effects in the manner described by EPA, and that EPA based its Reference Dose (RfD) principally on the work of the NAS/NRC (2005), and further that the NRC (2005) provided an insightful and conclusive discussion of perchlorate science, it is exceedingly clear that NRC did not use accepted risk assessment methods, nor EPA methods, to develop a reference dose. NRC concluded that hypothyroidism would be the first observed adverse effect, or critical effect (Faustman, and Omenn. 2001; EPA, 2008), and that the dose level at which this effect would likely first be observed (the no observed adverse effect level, or NOAEL) in healthy adults is 0.4 mg/kg-day. This choice might be appropriate basis of the RfD.

Yet, NRC selected the lowest of several precursors to this lowest adverse effect, the threshold of iodine uptake inhibition, as the starting point for its reference dose (RfD), because it was "more health protective". As NRC clearly stated, this effect of itself does not result in any harm, and the dose at which it occurs is approximately 100 times lower than the NOAEL of the first adverse effect. Moreover, this choice of lowest precursor is not consistent with EPA guidelines.

Specifically, NRC ignores two principles that govern calculating RfDs: 1. To identify an intake that "reduces hazard to a minimum and at the same time allows use of [necessary] chemicals ((Faustman, and Omenn. 2001)," and 2. To base RfDs on an adverse effect (Lehman and Fitzhugh, 1954), or an adverse effect or its precursor (Barnes and Dourson, 1988; EPA, 2002).

That is, the definition of critical effect by EPA specifies an adverse effect or its precursor---singular---meaning the penultimate precursor when several are available. Thus, the RfD has been, and must continue to be, the largest intake that can be reasonably certain to cause no injury to the whole

population. Otherwise, there is no reason not to choose lower precursors for any RfDs, resulting in RfDs that solely depend on how many precursor effects have been monitored.

The practice of focusing on the first adverse effect, or its known precursor, in dose response assessment, is based on decades of experience in the United States, Canada, and Europe. This practice allows us to draw conclusions about public health in the absence of observable data and in the presence of scientific uncertainty. The accepted process for developing RfDs (Barnes and Dourson, 1988) suggests two possible approaches to developing an RfD from the perchlorate data. The first would be to use the NOAEL of the critical effect from an adult population and apply uncertainty factors to account for sensitive populations and for lack of precision in defining this NOAEL. The second approach would be to use a NOAEL from a sensitive population.

Following this second approach, a standard RfD of 0.002 mg/kg-day has been described that is adequately health-protective (Strawson et al., 2004). This RfD may be suitably upgraded with the use of the newer epidemiology studies, as described briefly above.

Using a non-standard RfD process in regulating chemicals, such as that suggested by NAS (2005) for perchlorate, is not consistent with accepted EPA methods for developing such values. EPA's acceptance of this non-standard RfD undermines its good dose response assessment work in other programs.

Response: Please see the response to comment ID 20641 under comment code 2100, and the response to comment code 2100.

Commenter Name: Michael Dourson
Commenter Organization: Toxicology Excellence for Risk Assessment
EPA Document ID: EPA-HQ-OW-2008-0692-1562
EPA Comment ID: 20644
EPA Comment Code: 2100

Comment: However, we also recommend that EPA update its RfD prior to publishing a Health Advisory for the following reasons:

Additional important data on pregnant women and their offspring have become available since the time of the development of the EPA's RfD in 2005, which necessitate a reconsideration of the existing value. This reconsideration is consistent with recommendations of the NAS (2005) in its report.

The excellent relative source contribution evaluation of EPA, based on well supported and clearly described work of the FDA, necessitates a rethinking of the any RfD, since the underlying studies may not have measured perchlorate in the food of the human subjects.

The 2005 "RfD" of the NAS does not follow the existing EPA method.

Additional information is provided in the attached document.

Commentary on "Drinking Water: Preliminary Regulatory Determination on Perchlorate" Docket ID No. EPA-HQ-OW-2008-0068 Michael L. Dourson, Ph.D., DABT, ATS Joan Strawson, M.S., M.T.S.C., J.D. Toxicology Excellence for Risk Assessment (TERA)

The opinions expressed in this text are those of the authors for the purpose of protecting public health. These authors' opinions do not necessarily represent the views of the sponsors.

Response: See response to comment ID 20641 under response code 2100.

Commenter Name: Robert Howd
Commenter Organization: California Environmental Protection Agency, Water Toxicology Section
EPA Document ID: EPA-HQ-OW-2008-0692-1671
EPA Comment ID: 20646
EPA Comment Code: 2100

Comment: III (A)(1 and 2), pp 60266-60268. The NRC (2005) review of the Greer et al. (2002) study is discussed. EPA notes that the lowest dose of 7 ug/kg-day in the Greer et al. study corresponds to a statistical NOEL, and suggests that an uncertainty factor of 10 from the lowest dose is adequate to derive a health- protective level of 0.7 ug/kg-day, to account for human variability, as recommended by the NTP review panel. However, OEHHA would like to point out that the data also allow calculation of the lower confidence limit on a benchmark dose level for inhibition of iodide uptake. Using the lower 95% confidence limit of a 5% benchmark dose for inhibition of iodide uptake, OEHHA calculated a BMDL of 3.7 ug/kg-day, using EPA BMDS software (OEHHA, 2004). Although the low number of subjects (37) in the Greer et al. study cannot provide an accurate estimate of true human variability, it seems to us that using the available data in this calculation is a more reasonable way to account for the uncertainty in the data than just dividing the NOEL by 10. Our approach in fact follows the recommendations of EPA as to when BMD modeling should be applied.

It should also be noted that a sensitive population (women who consume low iodide levels) has been identified (Blount et al., 2006), and this population was excluded from the study of Greer et al. (2002). An apparent additional iodide inhibitory effect was noted by Steinmaus et al. (2007) in women who smoke (and consume low iodine). We therefore recommend that either the BMDL of 3.7 ug/kg-day be utilized for the calculation, or that an extra 3-fold uncertainty factor be utilized in the EPA NOEL/UF approach to account for the missing sensitive subpopulation and to help account for the known variability.

Because the NRC panel did not have access to the data of Blount et al. (2006), relying on the NRC conclusions without specific acknowledgement that that approach does not address the sensitive population issues seems inappropriate.

Response: See response to comment ID 20641 under comment code 2100. EPA agrees with the commenter's suggestions regarding the review and evaluation of additional new data regarding the health effects of perchlorate, and will do so as part of the perchlorate regulatory process.

Commenter Name: Brie Brigham
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-1436
EPA Comment ID: 20895
EPA Comment Code: 2100

Comment: The EPA has set an official reference dose of .0007 mg/kg/day of perchlorate, which is not expected to cause adverse health effects in humans. The EPA then converted this reference dose into a drinking water equivalent level of 24.5 ppb by assuming a person weighs 154 pounds and consumes 68 ounces of drinking water per day over a lifetime. Based on these conversions, the drinking water equivalent level for infants should be 4.35 ppb. The EPA assumes that a perchlorate contamination level of 15 ppb is safe. However, this level more than triples the level assumed safe for infants.

Response: The NRC (2005) identified "the fetus of pregnant women who might have hypothyroidism or iodide deficiency" as "the most sensitive population," but also identified infants and developing children as additional "sensitive populations." Infants and young children have greater exposure to contaminants in food and water because of greater consumption of food and water on a per unit body weight basis. See response to comment code 5220 for a discussion of alternative Health Reference Levels. National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276 p.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20900
EPA Comment Code: 2100

Comment: Compounding these problems, the CIIT relied heavily on a flawed, industry-funded study (the Greer study) when creating the computer model (Greer et al. 2002) - the problems with the Greer study have been documented in the published scientific literature and by the Massachusetts Department of Environmental Protection (Ginsberg and Rice 2005, MassDEP 2006).

Response: EPA believes that the Greer study, selected by the NRC as the basis for the RFD, represents the best available study for deriving a RfD. See response to comment code 2100.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20911
EPA Comment Code: 2100

Comment: The PBPK model relies heavily on industry-funded Greer study: The CIIT generated PBPK model uses data from the Greer study, which showed a dose-dependent decrease in iodine uptake (RAIU) by the thyroid gland with increasing perchlorate ingestion (Greer et al. 2002). This study included only 37 participants who were divided into several study groups and administered different doses of perchlorate for 14 days; the researchers determined that 0.007 mg/kg/day was the no observed effect level (NOEL) for perchlorate. The results from this study were used by the National Academy of Sciences (NAS) in setting the reference dose for perchlorate of 0.7 ug/kg/day.

However, the Greer study results and assumptions drawn from these results have been questioned in a peer-reviewed article that was published in Environmental Health Perspectives in 2005 (Ginsberg and Rice 2005). Two toxicologists, one from the Connecticut Department of Public Health and the other from the Maine Bureau of Health, conducted an analysis of the raw data from the Greer study and concluded that the "Individual results of Greer et al. point to an effect in four of the seven individuals tested at the lowest dose (0.007 mg/kg/day), indicating that this dose is an effect level." In other words, while Greer et al. and the NAS both concluded that 0.007 mg/kg/day is a NOEL, closer analysis of the data reveals that several of the 7 study subjects in this group experienced effects at this dose, thereby invalidating 0.007 mg/kg/day as a NOEL.

The Massachusetts Department of Environmental Protection (Mass DEP), which has set the most stringent drinking water standard for perchlorate nationally, had the following observations about the Greer study:

"MassDEP has concerns about the lowest dose in the Greer study being a no-effect level based on the facts that: due to the small number of subjects in the lowest dose group, there is low power to detect a statistically significant effect; averaging of group responses obscures positive individual inhibition; a non- statistically significant IUI (iodine uptake inhibition) effect was observed at the lowest dose tested; and, good low dose corroborating data is lacking" (MassDEP 2006).

In light of these valid criticisms of the Greer study, it is unclear why EPA chose to rely so heavily on the PBPK model that incorporates data from this study while essentially ignoring much more relevant data from the CDC.

Response: Blount et al., (2006) found that perchlorate exposure was a statistically significant predictor of thyroid hormones in women, but not in men. Their observations that adverse thyroid hormone effects were found in women whose urinary iodine was below 100 ug/L is suggestive of a partial study population iodine deficiency status. Blount et al. (2006) also noted several limitations of their study. Since their study was cross-sectional in design, it also cannot be concluded whether or not the association between perchlorate and thyroid hormone levels is causal, or is mediated by some other correlate of both. Blount et al., (2007) found that almost all participants in the same 2001-2002 NHANES survey, including the participants in their 2006 study, had urinary levels of perchlorate corresponding to estimated dose levels that are below the RfD of 0.7 ug/kg/day. The NRC recommended that data from the Greer et al. (2002) human clinical study be used as the basis for deriving a perchlorate reference dose (RfD) (NRC 2005), and also noted that the results of this study were supported by those of other human studies. From this Greer et al. (2002) human clinical study, the statistical no observed effect level (NOEL) for the perchlorate-induced inhibition of thyroid iodide uptake was determined to be 7.0 ug/kg (a corresponding iodide uptake inhibition of 1.8%). The NRC recommended that EPA apply an uncertainty factor of 10 to this NOEL of 7.0 ug/kg for the perchlorate-induced inhibition of thyroid iodide uptake, to account for differences in sensitivity between healthy adults and the most sensitive sub-population, consisting of fetuses of pregnant women who might have hypothyroidism or iodide deficiency.

EPA evaluated the published PBPK models (Clewell et al., 2007, and Merrill et al., 2005) and used them to further explore the relationship between water concentrations and iodide uptake inhibition in different subpopulations (USEPA, 2008). However, EPA did not rely on this PBPK analysis for determining the HRL. Rather, the HRL of 15 µg/l was calculated directly from the RfD to protect

the most sensitive subpopulation, the fetuses of pregnant women, using high end exposure assumptions. EPA thus applied the adjusted model to the HRL of 15 µg/l to determine the predicted percent RAIU inhibition (USEPA, 2008), and found that the 2.2 percent inhibition level for 7-day old bottle fed infants is comparable to the 1.8 percent inhibition level that the NRC identified as a no effect level in healthy adults and recommended as the point of departure for calculating the RfD (NRC, 2005). So, the modeling essentially agrees with the original NRC conclusions, and yielded results comparable to or below the 1.8 percent no effect inhibition level from the Greer (2002) study.

EPA used the best available peer-reviewed science, and the Agency has determined to regulate perchlorate in drinking water.

Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL. Environ Health Perspect. 2006 Dec;114(12):1865-71. Blount BC, Valentin-Blasini L, Osterloh JD, Mauldin JP, Pirkle JL. J Expo Sci Environ Epidemiol. 2007 Jul;17(4):400-7. Clewell RA, Merrill EA, Gearhart JM, Robinson PJ, Sterner TR, Mattie DR, Clewell HJ 3rd. J Toxicol Environ Health A. 2007 Mar 1;70(5):408-28. Greer MA, Goodman G, Pleus RC, Greer SE. Environ Health Perspect. 2002 Sep;110(9):927-37. Merrill EA, Clewell RA, Robinson PJ, Jarabek AM, Gearhart JM, Sterner TR, Fisher JW. Toxicol Sci. 2005 Jan;83(1):25-43. National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276pp. USEPA. 2008. Inhibition of the Sodium-Iodide Symporter By Perchlorate: An Evaluation of Lifestage Sensitivity Using Physiologically Based Pharmacokinetic (PBPK) Modeling. U.S. Environmental Protection Agency, Washington, D.C., 2009.

Commenter Name: Caroline Baier-Anderson, PhD
Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20945
EPA Comment Code: 2100

Comment: The EPA Reference Dose is not Adequately Protective of Human Health

The EPA Reference Dose is based on a Limited Study

The EPA Reference Dose for perchlorate is based on data from Greer et al. (2002) that observed the inhibition of radioiodide uptake. Ginsberg and Rice (2005) identified several problems with the Greer study that suggest the need for a reevaluation of the value that serves as the foundation for regulatory decision- making:

* Several individuals in the low dose group appear to demonstrate a response to perchlorate that is not evident in the reported mean. In analyzing this study, the National Academy of Sciences used the average response, and the significant variability in the response likely diminished the impact (e.g., as a result of reduced statistical power) of those showing a response.

* Ginsberg and Rice also point out that the apparent non-significant response resulted in the NAS characterizing the dose as a NOAEL, rather than a LOAEL. In their paper Ginsberg and Rice suggest an alternative interpretation that "[t]he data of Greer et al. (2002) point toward a more sensitive subgroup, which in this case represents more than half of the test group but is not evident

in the group mean analysis due to the variable nature of the response." If this is indeed the case then we can expect that there will be a wide range of susceptibility to perchlorate effects in the larger population.

Response: See response to comment ID 20641 under comment code 2100.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20957
EPA Comment Code: 2100

Comment: 2. The very particular case of perchlorate: Total effective perchlorate NOEL and RfD

-These food and drinking water perchlorate background levels are now known also for the U.S. population.

-These food and drinking water perchlorate background level are very low

-Therefore adding the background perchlorate level to the Greer (nominal) NOEL does not significantly increase the effective NOEL (from 7.0 to 7.04 ug/kg-day)

-However what significantly increases the nominal NOEL is the also known equivalent perchlorate background level caused by nitrate and thiocyanate and which results in an effective perchlorate equivalent NOEL of 12.8 ug/kg-day instead of 7 ug/kg-day.

Response: EPA believes that the Greer study as designed and interpreted by the authors is the appropriate interpretation. Addition of a correction for other sources would significantly bias the results. This is especially true given that the measured change in RAIU was a change relative to the start of the study, not an uncorrected measure. The use of the start of study measure effectively corrected for any background levels that existed on a subject by subject basis. Also, see response to comment code 2100.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20963
EPA Comment Code: 2100

Comment: The NRC RfD on itself was based on the Greer et al., 2002(1) critical study.

NRC believed that the Greer study cohort that had been administered the perchlorate dose-response doses, was, in terms of competitive iodine uptake inhibition caused by perchlorate (and, we suppose, by goitrogens in general), representative for the adult US population excluding the more sensitive subpopulations (The RfD took into account these subpopulations by applying an uncertainty factor, UF).

Conversely if this cohort would not have been representative for this (general) segment of the US population, the Greer study outcome wouldn't have been so either and therefore the resulting RfD couldn't have been assumed to be health protective for the US population either.

To our knowledge no argument has emerged that put in doubt the representativeness of the Greer cohort.

Response: EPA agrees.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20965
EPA Comment Code: 2100

Comment: The Greer study is a type 3 set-up (see section 1.3 below).

EPA asserts that it was applying a "default" RSC to estimate its former recommended DWEL (Drinking Water Equivalent Level) of 24.5 ppb issued in 2005 and based on the Greer study . With all due respect, EPA rather found that the RSC was not applicable for the reasons explained before. Indeed arriving at a 24.5 ppb DWEL from the RfD of 0.70ug/kg-day implies a RSC equal to 1 according to above equation with BW= 70 kg and DW =2l/day.

1.3. The Greer trial set-up

The Greer study cohort, in order to determine dose-response effects, received several oral doses of perchlorate.

Those doses were in addition to their background perchlorate levels originating from DW and food background sources.

The Greer trial was thus a type 3 set-up.

In fact the real NOEL for perchlorate alone (NOEL2) was not 0.7ug/kg-day as generally assumed but 0.7ug/kg-day plus the background from food + water. Thus in fact the 0.7ug/kg-day Greer NOEL (NOEL1) was an approximate or nominal level.

Establishing DW maximum contaminant levels based on trials where the contaminant is already consciously present in the background are not frequent but precedents do exist.

* The MCL of 2 ppm for barium was based on Wones R.G et al, Lack of Effect of Drinking Water Barium on Cardiovascular Risk Factors, Environmental Health Perspectives Volume 85, 1990, a critical human study, analogue to the Greer 2002.

We quote from Massachusetts Department of Environmental Protection:

http://www.mass.gov/dep/water/drinking/standards/barium.htm: "The MCLG is based on the RfD (presented below) derived from the Wones et al., study. It assumes that a 70 kg adult ingests 2

L/day of water. Since this value is based on a human study that considers contributions from food and air, no relative source contribution was applied for drinking water exposures"

* Also the nitrate MCL of 10 ppm N (as nitrate) was based on 2 critical human studies:

-Bosch H et al., (1950). Methemoglobinemia and Minnesota well supplies. Journal of the American Water Works Association 42:161-70, 1950 and

-Walton G (1951). Survey of literature relating to infant Methemoglobinemia due to nitrate contaminated water. Am. J. Public Health 41:986-96, 1951. There the RSC was considered as "not applicable" i.e. equal to 1.The RSC was not applicable because it did not have sense to apply it.

* The same reasoning went into the Cal. PHG (Public Health Goal) for fluorine: with an RSC = 100% followed by this

Comment: "OEHHA assumes that the populations under study exhibited comparable dietary and hygiene exposures to fluoride. Therefore, the relative source contribution factor is 100% to account for equal exposure of study populations to fluoride from sources other than drinking water (http://oehha.ca.gov/water/phg/pdf/fluor_c.pdf)

This is the same as saying that the study cohort was representative for the California population and that therefore the average background, which already contained fluorine, should have been so too.

Response: No response is necessary to the information provided by the commenter. Also, see response to comment code 2100.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20967
EPA Comment Code: 2100

Comment: B. The other goitrogens that are part of the background should be taken into account.

Most of the time, each contaminant has its own mode of action different from others or on different moments.

This is not the case for NIS (Sodium Iodine Symporter) related inhibitors of iodine uptake such as nitrate, perchlorate and thiocyanate which are competitive inhibitors with simultaneous joint effects (4).

Once again, to our knowledge this is the first time that background data are available also for the other goitrogens .This would allow to calculate an even more refined NOEL (NOEL4) and a corresponding HRL i.e. HRL4

In the Blount study those goitrogens were controlled for and evaluated when testing the relationship of perchlorate with T4 and TSH thyroid hormones. Average urinary(U) thiocyanate and nitrate levels were 1.2 (1.08-1.33 at 95% CI) and 38 mg/l (35.9-40.3 at 95% CI) respectively which, when

applying the relative potencies compared with perchlorate of 1/15 and 1/240(2) respectively, translated into 80 and 158 ug /L respectively.

80 ug /L U thiocyanate corresponds with about 2.8 ug/kg-day cyanide dietary uptake, applying the same regression as for perchlorate and assuming a 40% urinary recovery from cyanide and thioglucosides, the precursors of thiocyanate (5, 6).

158 ug /L U nitrate corresponds with about 3.0 ug/kg-day nitrate dietary uptake, applying the same regression as for perchlorate and assuming a 75 % urinary recovery (7, 8).

The total average perchlorate equivalent background is therefore estimated at 0.04 + 2.8 + 3.0 =5.8 ug/kg-day.

This comes down to trial set-up type 3 instead that the DW perchlorate BG plus the perchlorate equivalent BG should be added to the RfD and with RSC =1 since all contributors are now captured in the effective total equivalent NOEL (= NOEL4) and RfD (=RfD4) as shown in the following equations and fig.4 :

NOEL4= NOEL1 dose +FBG+ DWBG + PEBG.

RfD4= NOEL4/UF= NOEL4/10

HRL4 = [(RfD3 +PEBG) Ã— BW)/DWI] Ã— RSC= [(RfD4) Ã— BW)/DWI] x 1

Fig. 4: NOEL based on dose-response trial with perchlorate food background and with drinking water background: perchlorate equivalent background. [see PDF Docket ID EPA-HQ- OW-2008-0692-1798]

So the background levels of the other 2 goitrogens are substantially more relevant than the perchlorate back ground level itself.

This increases the effective perchlorate equivalent NOEL (NOEL4) to 7 ug/kg-day +5.8 ug/kg-day = 12.8 ug/kg-day which would have lead to a total goitrogen RfD4 of 1.28 ug/kg-day and a DW HRL4 of 44.8 ppb for perchlorate and nitrate/240 together (Thiocyanate in DW is negligible in the absence of a point source contamination).

Indeed when applying an RSC =1, BW= 70kg and DWI = 2 l/day, the HRL equation becomes:

HRL4 = [(RfD4 Ã— BW)/DWI] Ã— RSC = 44.8 ppb =45 ppb

So the perchlorate equivalent effect due to the other 2 goitrogens has a much larger impact on the final optimal HRL (HRL4) than the perchlorate background itself but has not been taken into consideration.

Response: While EPA acknowledges that nitrate and thiocyanate have the same mode of action as perchlorate, and that the effects of combined exposure to perchlorate, nitrate, and thiocyanate are additive, EPA does not believe there are sufficient scientific data currently available to assess and characterize the combined risk of these contaminants. EPA has committed to a drinking water

strategy that outlines four principles to expand public health protection for drinking water. One of these principles is to address contaminants as groups. However, EPA does not believe that regulatory action to address perchlorate should be further delayed. Therefore, EPA intends to develop a proposed rule for perchlorate. At such time as a NPDWR is promulgated, EPA is required to review and revise, as appropriate, its drinking water standards at least every six years. Any revision must at least maintain or improve public health protection. When there are sufficient scientific data to assess the cumulative risks of perchlorate and other contaminants, EPA will review this information to evaluate whether any new or revised NPDWRs are appropriate.

Commenter Name:
Commenter Organization: Ag Council et al
EPA Document ID: EPA-HQ-OW-2008-0692-1987
EPA Comment ID: 20975
EPA Comment Code: 2100

Comment: The NAS Study is the Most Comprehensive Scientific Review on the Health Effects of Perchlorate to Date.

We support EPA's decision to rely on the recommendations of the NAS perchlorate review panel in deriving a reference dose (RfD). From our perspective, the NAS panel conducted a thorough scientific inquiry of the available health effects literature in a highly professional and independent manner. The Panel's 2005 recommendations, based upon the best science then available, continue to be validated by new scientific studies on perchlorate health effects and exposures. It is critically important to bear in mind that the NAS panel views the perchlorate RfD as providing a large margin of safety because it is based on a No-Observed-Effect-Level (NOEL) as opposed to EPA's traditional approach of deriving the RfD from a No-Observed-Adverse-Effect-Level (NOAEL). The NOEL is a precursor effect (inhibition of iodine uptake by the thyroid) to an actual adverse effect (hypothyroidism). The RfD also incorporates a 10-fold safety factor to account for variability in the human population. For these reasons, the NAS views the RfD as highly health protective, even for sensitive subpopulations.

Response: See response to comment code 2100.
Greer MA, Goodman G, Pleus RC, Greer SE. Health effects assessment for environmental perchlorate contamination: the dose response for inhibition of thyroidal radioiodine uptake in humans. Environ Health Perspect. 2002 Sep;110(9):927-37. Erratum in: Environ Health Perspect. 2005 Nov;113(11):A732. National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276pp.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20984
EPA Comment Code: 2100

Comment: A reference dose (RfD) is an estimate of the daily exposure to an agent over a full lifetime that is "likely to be without an appreciable risk of deleterious effects" for the human

population, including sensitive subgroups.[FN13: EPA Integrated Risk Information System (IRIS) Glossary of terms. http://www.epa.gov/ncea/iris/help_gloss.htm#r] In 2005, the National Research Council (NRC) of the National Academy of Sciences recommended an RfD for daily intake of perchlorate that it considered to be an acceptable level of exposure of 0.7 ug/kg/day.[FN14: NRC. 2005. Health Implications of Perchlorate Ingestion. National Research Council of the National Academies. National Academies Press, Washington, D.C.] EPA adopted this RfD and posted on its public database, the Integrated Risk Information System (IRIS) in February 2005.[FN15: EPA IRIS assessment of perchlorate. http://www.epa.gov/NCEA/iris/subst/1007.htm]

Response: No response is necessary to the information provided by the commenter. Also, see response to comment code 2100.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20986
EPA Comment Code: 2100

Comment: The RfD for perchlorate and perchlorate salts of 0.7 ug/kg body weight/day is based on a human volunteer study, Greer et al, 2002.[FN16: Greer, M.A., Goodman, G., Pleuss, R.C., Greer, S.E. 2002. Health effect assessment for environmental perchlorate contamination: The dose response for inhibition of thyroidal radioiodide uptake in humans. Environ. Health Perspect. 110:927-937.] The RfD is for oral exposure, including food and water, and is based on radioactive iodide uptake inhibition (RAIU) in the thyroid as the critical effect. The IRIS assessment of perchlorate explains that "The point of departure is based on a non-statistically significant mean 1.8% (standard error of the mean 8.3%) decline in RAIU in healthy adults following two weeks exposure to a daily perchlorate dose of 0.007 mg/kg/day. An intraspecies uncertainty factor of 10 is applied to protect the most sensitive population, the fetuses of pregnant women who might have hypothyroidism or iodide deficiency. Dose is given as perchlorate anion."[FN17: EPA. IRIS database. Perchlorate and perchlorate salts. http://www.epa.gov/ncea/iris/subst/1007.htm#revhis]

Response: No response is necessary to the information provided by the commenter. Also, see response to comment code 2100.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20987
EPA Comment Code: 2100

Comment: The RfD adopted by EPA has been widely criticized as inadequately protective by state scientific experts[FN18: Ginsberg G and D Rice. The NAS perchlorate review: questions remain about the perchlorate RfD. Environ Health Perspect. 2005 Sept; 113(9):1117-9. Erratum in: Environ Health Perspect. 2005 Nov; 113(11):A732.] and by EPA's own Children's Health Protection Advisory Committee,[FN19: Letter from Melanie Marty to Administrator Johnson regarding Preliminary Regulatory Determination on Perchlorate (November 3, 2008, PDF) http://yosemite.epa.gov/ochp/ochpweb.nsf/content/perchlorateletter.htm/$file/Per

chlorateLetter.pdf] and no longer reflects the best available data.[FN20: EN Pearce, AM. Leung, BC Blount, HR Bazrafshan, X He, S Pino, L Valentin-Blasini, and LE Braverman, 2007. Breast milk iodine and perchlorate concentrations in lactating Boston-area women. J Clin Endocrinol Metab. 92(5):1673-7.] [FN21: Letter from Melanie Marty to Administrator Johnson regarding Preliminary Regulatory Determination on Perchlorate (November 3, 2008, PDF) http://yosemite.epa.gov/ochp/ochpweb.nsf/content/perchlorateletter.htm/$file/PerchlorateLetter.pdf] However, even when basing its decision upon this unacceptably high RfD, EPA's preliminary determination not to regulate perchlorate would still expose hundreds of thousands of children and infants to unsafe levels of perchlorate.

Response: EPA respectfully disagrees with the commenter. See response to comment code 2100.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20994
EPA Comment Code: 2100

Comment: D. EPA relies on the RfD based on the comparatively weak Greer et al study to determine the HRL

In simple terms, the HRL is the maximum tolerable amount of perchlorate that could be in drinking water, considering that perchlorate is also in food, and still keep daily consumption levels from exceeding the RfD. The HRL was calculated as follows: For all populations, including pregnant women, EPA determined that the RfD is 0.7 ug/kg/day. This value is posted on the IRIS database based on recommendations from a committee of the National Academies. EPA reports that for pregnant women, exposure to perchlorate from food is 0.263 ug/kg/day at the 90th percentile (based on data from a national food survey), representing nearly 38% of the RfD, thus leaving an RSC (relative source contribution) for water of 62% (FR at 60276). This is equivalent to 0.437 ug/kg/day from water, assuming an average body weight of 70 kg, and a daily water consumption of 2 L (90th percentile adult water consumption). That is, 0.437 ug x 70 kg body wt. = 30.6 ug perchlorate in 2 L (the daily consumption amount). This is 15 ug/L, or 15 ppb, the HRL.

Because the dose-response relationship used to determine the RfD is derived exclusively from the Greer et al study, the HRL also is dependent on the Greer et al study to determine the maximum allowable level of drinking water contamination.

The Greer et al study [FN34: Greer MA, G Goodman, RC Pleus, and SE Greer. 2002. Health effects assessment for environmental perchlorate contamination: the dose- response for inhibition of thyroidal radioiodine uptake in humans. Environ Health Perspect 110:927-937.] reported on study results from intentional dosing of a small population (N=37) of healthy men and women, for only two weeks, and the study lacked measurements of iodine status that is now known to be a critical variable. Other serious problems with the Greer study included the fact that the low dose group contained only seven participants including only six women. Use of these limited data to calculate a regulatory trigger level has been widely criticized as inadequate by state scientific experts[FN35: Ginsberg G and D Rice. The NAS perchlorate review: questions remain about the perchlorate RfD. Environ Health Perspect. 2005 Sept; 113(9):1117-9. Erratum in: Environ Health Perspect. 2005 Nov; 113(11):A732.] and by EPA's own Children's Health Protection Advisory

Committee,[FN36: Letter from Melanie Marty to Administrator Johnson regarding Preliminary Regulatory Determination on Perchlorate (November 3, 2008, PDF) http://yosemite.epa.gov/ochp/ochpweb.nsf/content/perchlorateletter.htm/$file/PerchlorateLetter.pdf] and no longer reflects the best available data.[FN37: EN Pearce, AM. Leung, BC Blount, HR Bazrafshan, X He, S Pino, L Valentin-Blasini, and LE Braverman, 2007. Breast milk iodine and perchlorate concentrations in lactating Boston-area women. J Clin Endocrinol Metab. 92(5):1673-7.][FN38: Letter from Melanie Marty to Administrator Johnson regarding Preliminary Regulatory Determination on Perchlorate (November 3, 2008, PDF) http://yosemite.epa.gov/ochp/ochpweb.nsf/content/perchlorateletter.htm/$file/PerchlorateLetter.pdf] Despite these limitations, careful analysis of the Greer data reveal clear evidence of perchlorate toxicity in the low-dose group; three subjects showed no perchlorate effect, but four subjects in the low-dose group had a measurable decrease in iodide uptake commensurate with perchlorate exposure.[FN39: For a complete analysis of the NAS review of perchlorate, see: Ginsberg G and D Rice. The NAS perchlorate review: questions remain about the perchlorate RfD. Environ Health Perspect. 2005 Sept; 113(9):1117-9. Erratum in: Environ Health Perspect. 2005 Nov; 113(11):A732.] Because the study authors relied on averaged data rather than individual data, the more sensitive individuals in the study group were obscured

The short duration of the Greer study, only 14 days, creates considerable uncertainty that the cumulative effect of longer-term exposure are accounted for. A study in rats found greater perchlorate toxicity to the thyroid from 90- day exposure than from 14-day exposure (Springborn Laboratories 1998), suggesting that cumulative exposure may cause significant systemic injury that is not detectable in a short-term study. Although one longer-term (six month) human study with 13 volunteers has been promoted by industry as indicating that humans adapt to long-term exposure (Braverman et al. 2006[FN40: Braverman LE, EN Pearce, X He, S Pino, M Seeley, B Beck, B Magnani, BC Blount, and A Firek. 2006. Effects of six months of daily low-dose perchlorate exposure on thyroid function in healthy volunteers. J Clin Endocrinol Metab. Jul; 91(7):2721-4. Epub 2006 Apr 24.]) this study was unlikely to have adequate statistical power to detect an effect, especially given the particular vulnerability for some populations. The Blount (2006) study showed that some people are much more vulnerable to perchlorate toxicity than the average population; women are more sensitive than men, iodine-deficient women are more sensitive than iodine-sufficient women, and iodine-deficient women with TSH levels on the high end of the normal range are even more sensitive than other iodine-deficient women.[FN41: Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environ Health Perspect. 2006 Dec;114(12):1865-71.] Other human studies suffer from the same limitations. For example, a study of chronically perchlorate-exposed pregnant women in Chile[FN42: Tellez RT, PM Chacón, CR Abarca, BC Blount, CB Van Landingham, KS Crump and JP Gibbs. 2005. Long-term environmental exposure to perchlorate through drinking water and thyroid function during pregnancy and the neonatal period. Thyroid 15(9):963-975.] that also failed to find an effect of perchlorate exposure had only three iodine- deficient female subjects out of 183.

Response: Regarding this comment encouraging EPA to review additional data to support the perchlorate regulatory determination, EPA will continue to rely on the best available science as it proceeds through the rulemaking process.

Please see the response to comment ID 20987 under comment code 2100, and the response to comment code 2100 for a discussion of the RfD. Please see the response to comment code 5220 for a discussion of alternative Health Reference Levels.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20999
EPA Comment Code: 2100

Comment: EPA tries to support its conclusions that the HRL is safe by avoiding referring to the RfD, and instead referring to the level of inhibition of RAIU on which the NRC report (NRC, 2005) based its recommended RfD.[FN54: 73 Fed. Reg. at 60277.] EPA cannot pretend that its own RfD does not exist, and shift its evaluation of acceptable exposure estimates to a discrete biological endpoint.

Response: Please see the response to comment code 5220 for a discussion of alternative Health Reference Levels. Please see the response to comment ID 20987 under comment code 2100, and the response to comment code 2100.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-2082
EPA Comment ID: 21022
EPA Comment Code: 2100

Comment: 5. Your letter also raises concerns with the Greer et al. study, stating that the RfD is uncertain and not necessarily a health protective benchmark because Greer was a short-term study with a small sample size.

The NAS perchlorate panel addressed this very issue at length in their comprehensive report, pointing out that there were four doses across 37 subjects. Second, the panel concluded that since the point of departure is based upon IUI- a short-term event- any chronic effects "would have no greater effect" than any short term effects that may occur (NAS, 2005). Importantly, the NAS also noted that it did not examine Greer in isolation. The NAS noted that the findings in Greer are supported by other clinical studies, occupational and environmental epidemiological studies, and studies of long-term perchlorate administration to patients with hyperthyroidism. ATSDR reviewed all the literature in its 2008 toxicology document and still agrees that Greer et al. (2002) is the best study to determine a point of departure for a toxicity guideline value.

Response: Please see response to comment code 2100.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21056
EPA Comment Code: 2100

Comment: [Text Box: On basing an RfD on a no effect level for a non adverse effect, the NRC states: "Inhibition of iodide uptake by the thyroid clearly is not an adverse effect; however if it does not occur, there is no progression to adverse health effects."]

For this current regulatory determination, EPA has the benefit of a rigorous and independent peer review of the available science. These include the study by the NRC and more recently the Agency for Toxic Substances and Disease Registry, an agency of the Department of Human Health Services (ATSDR, 2008).

In 2005, the NRC perchlorate panel reached a consensus and recommended an RfD of 0.0007 mg/kg per day. The NRC panel comprised 15 leading scientists and physicians with wide-ranging expertise necessary to evaluate all aspects of the available science related to perchlorate. The NRC process occurred over a 15- month time period, providing ample time for the panel to review studies and consider oral testimony and written comments prior to issuing its conclusions and recommendations. As part of this process, the NRC panel performed an exhaustive review of the wide body of available animal and human studies as well as other scientific data relevant to understanding the health effects of perchlorate. The NRC panel noted that "emphasis was given to studies with the soundest scientific methods to draw conclusions regarding the effects of perchlorate exposure" (NRC, 2005).

The charge to the Committee was to "critically evaluate the scientific literature, including both human and animal data, and...assess the key studies underlying EPA's 2002 Draft Toxicological Review and Risk Characterization for Perchlorate in terms of quality, reliability, and relevance to draw conclusions about the health implications of exposure to low levels of perchlorate in drinking water." As stated in the NRC Committee Report, "EPA has been criticized that it did not appropriately consider all the relevant data for its assessments and that it based its conclusions on flawed scientific studies" (NRC, 2005).

The NRC independently evaluated the science which was published in the report Health Implications of Perchlorate Ingestion (2005). The NRC report recommended an RfD of 0.7 ug/kg-d based on a No Observed Effect Level (NOEL), or the dose at which no effects occur, adverse or otherwise (NRC, 2005). One of the critical studies that served as the basis for this RfD was the study by Greer et al. (2002) which demonstrated that there was no inhibition of iodide uptake by the thyroid at a dose of 7 ug/kg-d. Importantly, the NRC did not examine Greer in isolation. According to the NRC report, the findings in Greer are supported by other clinical studies, occupational and environmental epidemiologic studies, and studies of long-term perchlorate administration to patients with hyperthyroidism.

Further, the NRC states with emphasis, "Inhibition of iodide uptake by the thyroid clearly is not an adverse effect; however if it does not occur, there is no progression to adverse health effects." The committee views its recommendation to use [IUI] by the thyroid as the basis of the perchlorate risk assessment to be the most health-protective and scientifically valid approach (NRC, 2005).

[Text Box: After review all scientific data, including studies since the release of the NRC perchlorate review, ATSDR has adopted the EPA's chronic RfD recommended by the EPA (2005) for the chronic MRL"]

In using a NOEL, the NRC committee was conservative as this dose is already lower than any dose in which adverse effects occur; a safety factor of 10 is further applied to the already conservative NOEL to account for the most sensitive individuals in a population, in this case, hypothyroid or iodine- deficient pregnant women and their developing fetuses. The NRC panel stated that using a NOEL as the point of departure is a more conservative and health- protective approach than EPA's customary approach of using the adverse effect (NRC, 2005). Thus, for example, the use of IUI as a point of departure is a more cautious health protective approach than using changes in thyroid hormones (a precursor to possible adverse effects) or to some adverse effect such as hypothyroidism.

The panel also took time to differentiate between a NOAEL and a NOEL, finding that there was confusion between the two and stating that the NOAEL is based upon an adverse effect, whereas the NOEL is based upon a nonadverse effect (NRC, 2005). With the incorporation of an uncertainty factor of 10, the RfD recommended by the NRC was many times lower than the point at which adverse effects occur. It should be noted that the NRCNRC report concluded that no other uncertainty factors were necessary. Specifically on the issue of adequacy of database, the NRC concluded that the database contained sufficient studies from which to determine an RfD, finding that the database contained both human and animal data from which to evaluate IUI. The NRC also concluded that no LOAEL to NOAEL conversion factor was required, since the point of departure was the NOEL, again, a more conservative approach. Some have also argued that the Greer study was of short duration and have argued for a subchronic to chronic extrapolation. On that issue, the NRC concluded that since the point of departure is based upon IUI-a short-term event-any chronic effects "would have no greater effect" than any short term effects that may occur. (NRC, 2005).

The EPA has based its RfD for perchlorate and Integrated Risk Information System (IRIS) summary on the NRC report.

Response: No response is necessary to the information provided by the commenter. Also, see response to comment code 2100.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21059
EPA Comment Code: 2100

Comment: It should be noted that the RfD aims to protect the most sensitive individuals within a population (i.e., pregnant women and their fetuses). While some have argued that the infant or child is the more sensitive individual in the population; the experts of the Perchlorate NRC committee, EPA, ATSDR, OEHHA, and others, disagree. In addition, no reliable scientific data at relevant environmental exposures for this change in sensitive population has been put forward. One of the central considerations in these arguments is the disregard of dose and exposure. Any chemical at a sufficient dose will cause an adverse effect.

[Text Box: Studies published since the NRC report in 2005 add to an already well-developed database, adding more studies that are consistent to previous analyses and reducing uncertainty. Thus, the science supports EPA's decision that the current RfD for perchlorate is both conservative and health protective to even the most sensitive individuals.]

However, dose is a foundational tenant of the standard medical sciences (e.g., toxicology, endocrinology, pharmacology, etc.). Dose consideration is an absolute foundation of the risk assessment process by all recognized authoritative bodies.

Response: See response to comment code 2100.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21067
EPA Comment Code: 2100

Comment: First, as stated above, ATSDR (2008) reviewed this study in their assessment and did not feel that it merited any special consideration over other studies in the well developed perchlorate literature database. They state that their decision "...was made after a careful evaluation of the NRC report and of studies that have been published after the NRC (2005) report. The results from newer studies do not change the bottom-line recommendation" (ATSDR, 2008).

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21094
EPA Comment Code: 2100

Comment: EPA has provided sufficient support for its findings under the SDWA. To take the statutory criteria in turn:

May perchlorate have an adverse effect on the health of persons?

Everything - including water itself - may cause an adverse effect if the dose is sufficiently high. The plain meaning of the first criterion relates to the dose of the contaminant at levels which people are likely to be exposed to through drinking water.

The scientific literature is clear that perchlorate will not cause adverse effects at the concentrations under review here. The NAS report declares,

An important point is that inhibition of thyroid iodide uptake is the only effect that has been consistently documented in humans exposed to perchlorate. The continuum of possible effects of iodide-uptake inhibition caused by perchlorate exposure is only proposed and has not been demonstrated in humans (with the exception that in patients with hyperthyroidism doses of 200 mg daily or higher may reduce thyroid secretion). More importantly, the outcomes at the end of the continuum are not inevitable consequences of thyroid exposure.

In other words, except for its deliberate medical use, perchlorate has never been shown to have caused adverse effects in humans. Moreover, the NAS also concluded that perchlorate is not likely to be a carcinogen.

In addition to the NAS conclusions, subsequent studies indicate perchlorate has not been demonstrated to have an adverse effect on the health of persons at environmentally relevant levels (Blount et al., 2006). The weight-of-evidence suggests that adverse effects do not occur following chronic exposures to perchlorate at doses much greater than the RfD (Tellez et al., 2005; Amitai et al., 2006; Braverman et al., 2006).

Response: EPA's final determination to regulate perchlorate is based upon the National Research Council's 2005 (NRC, 2005) recommendation to use data from a human clinical study (Greer et al. 2002) as a basis for the human health risk assessment, and as a basis for the RfD. On August 19, 2009, EPA published a FR Notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (FR Vol. 74, No. 159, p. 41883). In this August 19, 2009 FR Notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard. EPA has considered and discusses in the FR Notice the results of current scientific literature on potential adverse biochemical effects, in the process of evaluating the adverse human health effects of perchlorate. See response to comment code 2100.

Greer MA, Goodman G, Pleus RC, Greer SE. Health effects assessment for environmental perchlorate contamination: the dose response for inhibition of thyroidal radioiodine uptake in humans. Environ Health Perspect. 2002 Sep;110(9):927-37. Erratum in: Environ Health Perspect. 2005 Nov;113(11):A732. National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276pp.

Commenter Name: Ellen Blaschinski, M.B.A., R.S.
Commenter Organization: Regulatory Services Branch, Connecticut Department of Public Health
EPA Document ID: EPA-HQ-OW-2008-0692-2091
EPA Comment ID: 21114
EPA Comment Code: 2100

Comment: November 21, 2008 Water Docket Environmental Protection Agency Mailcode 2822T 1200 Pennsylvania Ave, NW Washington DC 20460 Re: Docket 1D No. EPA-HQ-OW-2008-0692

The Connecticut Department of Public Health appreciates this opportunity to comment on the Agency's Preliminary Regulatory Determination for Perchlorate dated Oct 10, 2008. We have been following perchlorate closely because of its toxic properties and widespread occurrence in the human environment, particularly in food and water supplies impacted by local sources. It appears that risks from perchlorate in drinking water could be appreciable during the perinatal period in cases where iodine intake is marginal. This concern comes from the CDC study showing that perchlorate body burden is correlated with decreased thyroid hormone levels in the 31% of US women with low iodide intake (Blount et al. Environ Health Perspect 114:1865, 2006). Given the sensitive relationship between thyroid hormone and brain development, it is critical that the perinatal period be adequately protected from agents which can interfere with thyroid hormone

production. Therefore, regulting perchlorate in drinking water represents a meaningful opportunity for EPA to safeguard public health by setting a health-protective Maximum Contaminant Level (MCL) and then by requiring water supplies to regularly rest for this analyte.

Response: Please see the response to comment ID 20975 under comment code 2100.

Commenter Name: John P Gibbs
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0636
EPA Comment ID: 28550
EPA Comment Code: 2100

Comment: My comments are in the attached file.

John P Gibbs, MD 300 Fischer Store Road Wimberley,TX 78676 phone 512/847-2748 cell: 512/667-0625 email jpgibbs@hughes.net

ENVIRONMENTAL PROTECTION AGENCY OFFICE OF WATER [EPA-HQ-OW-2009-0297; FRL-8943-9], RIN 2040-AF08 Drinking Water: Perchlorate, Supplemental Request for Comments Federal Register / Vol. 74, No. 159 / Wednesday, August 19, 2009 / Notices

Water Docket, EPA Docket Center (EPA/DC) EPA West, Room 3334, 1301 Constitution Ave., NW, Washington, DC. (202) 566-2426.

Dear Sirs,

I appreciate the opportunity to comment on the United States Environmental Protection Agency (U.S. EPA) Office Water regarding its request for supplemental comments. I have been very active with the perchlorate issue over the past 11 years.

John P. Gibbs, MD PO Box 2948, 300 Fischer Store Road Wimberley, Texas 78676 Phone: 512-847-2748, cell 512-667-0625 Email: jpgibbs@hughes.net

1) The 2005 NAS REPORT

Perchlorate is one of the most well-studied chemicals with detailed information on the mechanism of action, dose-response, and health effects. The 2005 NAS report was a comprehensive review of the science. The animal and human studies that have been published since the NAS report reduce the uncertainty and reinforce the NAS panel's finding that there will not be any adverse health effects from perchlorate at environmentally-relevant concentrations

In using a NOEL, the NAS committee deemed its approach as conservative and health protective as this dose is already lower than any dose in which adverse effects occur. Furthermore, a safety factor of 10 is applied to the NOEL to account for the most sensitive individuals in a population, in this case, hypothyroid or iodine-deficient pregnant women and their developing fetuses. The NAS panel stated that "the NOEL value from Greer et al. (2002) is a health- protective and conservative point of departure is supported by...extensive human and animal data that demonstrate that there will be no progression to adverse effects if no inhibition of iodide uptake occurs"

Response: For the reasons provided in the preliminary and final determinations, EPA has found that perchlorate may have an adverse effect on human health. Also, see response to comment code 2100.

Commenter Name: John P Gibbs
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0636
EPA Comment ID: 28554
EPA Comment Code: 2100

Comment: 5) CONCLUSIONS

The 2005 NAS report remains the most credible and complete assessment on potential toxicity of perchlorate from environmental sources. All scientific reports issued after the NAS report (with the exception of Blount et al 2006) support that the RfD recommended by the NAS is protective for sensitive subpopulations. Setting an MCL for perchlorate in drinking water below 15 or 24 ug/L does not provide meaningful opportunity for improving public health.

Response: EPA has considered the results of current scientific literature on potential adverse biological effects, in the process of evaluating the adverse human health effects of perchlorate. The Agency analyzed the additional information, and EPA has determined that a national primary drinking water regulation for perchlorate would present a meaningful opportunity for health risk reduction for persons served by public water systems, and that regulation of perchlorate in drinking water due to occurrence and health implications is warranted. EPA will continue to evaluate all of the available science related to perchlorate as the Agency develops a National Primary Drinking Water Regulation for perchlorate. See response to comment code 5220 for a discussion of alternative Health Reference Levels.

Commenter Name: Sonia Salas
Commenter Organization: Western Growers Association on behalf of several California agriculture groups
EPA Document ID: EPA-HQ-OW-2009-0297-0652
EPA Comment ID: 28678
EPA Comment Code: 2100

Comment: The NAS Report Remains the Most Comprehensive Scientific Review on the Health Effects of Perchlorate to Date.

The National Academy of Sciences conducted a thorough inquiry of the perchlorate health effects literature in a highly professional and independent manner. The Panel's 2005 recommendations, based upon the best science available, continue to be validated by new scientific studies on perchlorate health effects and exposures. It is critically important to bear in mind that the NAS panel views its recommended perchlorate reference dose (RfD) as providing a large margin of safety because it is based on a No-Observed-Effect-Level (NOEL) -- inhibition of iodine uptake by the thyroid - rather than the traditional approach of starting from a No-Observed-Adverse-Effect-Level (NOAEL). The NOEL is the level below which exposure to a substance fails to elicit any biological response at all, and in the case of perchlorate is orders of magnitude below the levels at which

adverse effects may occur. The NAS perchlorate panel further reduced this NOEL by a factor of 10 to account for variations in human response, leading them to conclude that their recommended RfD is highly health protective, even for sensitive subpopulations.

Further downward adjustment of the RfD based on body weight and water consumption rates at various life stages, as contemplated in EPA's proposed alternative health reference levels, is needlessly duplicative and provides no additional health protection for any population. Moreover, EPA has not presented any scientific evidence indicating why its current perchlorate health reference level (15 ppb), which is based on the most sensitive sub-population (the pregnant woman/fetus), and which incorporates a ten-fold safety factor to account for variability in human response, is inadequate.

Response: See response to comment code 5220 for a discussion of alternative Health Reference Levels.

Commenter Name: Kay Brothers
Commenter Organization: Southern Nevada Water Authority
EPA Document ID: EPA-HQ-OW-2009-0297-0667
EPA Comment ID: 28695
EPA Comment Code: 2100

Comment: The NRC perchlorate panel (2005) and the EPA agreed that the most susceptible population are "the fetuses of pregnant women who might have hypothyroidism or iodide deficiency" but also identified infants and developing children as additional "sensitive populations." Epidemiological data shows that at perchlorate exposures above and below the EPA's Reference Dose (RfD) for perchlorate, no adverse health effects were documented in adults and children exposed chronically to perchlorate via drinking water (Crump and Gibbs 2005; Tellez, Chacon et al. 2005; Amitai, Winston et al. 2007).

Response: See response to comment code 2100 and today's Federal Register notice for a discussion of EPA's finding of possible adverse health effects.

Commenter Name: Robert E. Brackett
Commenter Organization: Grocery Manufacturers Association (GMA)
EPA Document ID: EPA-HQ-OW-2009-0297-0413
EPA Comment ID: 28707
EPA Comment Code: 2100

Comment: Second, EPA must make it clear to the public that the starting point for determining the Reference Dose (RfD), a safe daily exposure level for perchlorate, is a biological effect that is not itself harmful, and does not indicate any harm will occur. In 2005, an expert panel of the National Research Council (NRC) reviewed the evidence and determined a reference dose (RfD) for perchlorate based on a No Observed Effect Level (NOEL) in a study in human subjects. The NOEL is the lowest observed dose at which no biologically significant changes are observed, and it is a lower does than the customary starting point for an RfD, the No Observed Adverse Effect Level (NOAEL), the dose at which no adverse effects are observed. Humans and animals have built-in, compensatory mechanisms that assure their survival over a wide range of complex and continually changing challenges. Biological changes that are part of these normal compensatory

mechanisms are considered adaptive, not adverse. The NRC experts specifically articulated that extra measure of protection inherent in their use of the NOEL. In addition, they used a safety factor of 10 to account for any variations in sensitivity within the population potentially at risk, hypothyroid or iodine deficient pregnant women and developing fetuses. The NRC approach assures that, even if the sensitive population were to experience an exposure as high as the RfD there is a high degree of confidence that no adverse effects will occur.

Response: EPA believes the NRC appropriately based the RfD on iodide uptake inhibition to the thyroid, for the reasons discussed in its report. EPA notes that the data underlying the definition of iodide uptake inhibition as a precursor effect and the relationship of iodide uptake inhibition to the continuum of adverse outcomes reflects an understanding of effects in adults; it may not reflect the relationship of the precursor event to adverse outcomes in neonates and infants, who may not have iodide stores sufficient to offset the effects of reduced iodide uptake. The less resilient neonatal and infant system makes the exposure gap between a precursor event (iodide uptake inhibition due to perchlorate) and reduced T3/T4 levels likely to be narrower than for adults, and in fact, the distinction between the two may be blurred for the very young (Greer et al., 2002; Savin et al., 2003; van den Hove et al., 1999). The NRC noted that, "[T]he minimal prolonged decrease in thyroid hormone production that would be associated with adverse health effects is not known; any decrease is potentially more likely to have adverse effects in sensitive populations (people with thyroid disorders, pregnant women, fetuses, and infants) but data are not available to determine the magnitude of the decrease needed to cause adverse effects in those populations."

Commenter Name: Nsedu O. Witherspoon
Commenter Organization: Children's Environmental Health Network
EPA Document ID: EPA-HQ-OW-2009-0297-0674
EPA Comment ID: 28740
EPA Comment Code: 2100

Comment: Moreover, a 1 ppb or lower MCL is supported by the most recent comprehensive studies, and these should be central to EPA's analysis. The industry-supported Greer study, which serves as the basis for EPA's current reference dose as well as California's current 6 ppb standard, consisted of a 14-day study of 37 healthy adults. In more recent years, Blount et al analyzed a nationally representative sample of 2299 U.S. residents, and they have documented anti- thyroid effects in a large population of women exposed to perchlorate at concentrations far lower than levels previously shown to have such effects. This study and subsequent data clearly justify promulgation of an even more protective MCL. It should be noted that California's Office of Environmental Health Hazard Assessment is in the process of reevaluating its Public Health Goal, on which the state MCL is based.

Response: See response to comment code 5220 for a discussion of alternative Health Reference Levels and response to comment code ID 28936 under comment code 2100 for a discussion of the Blount et al study. EPA will conduct further analysis in developing a proposed MCL and MCLG for perchlorate.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28794

EPA Comment Code: 2100

Comment: A reference dose (RfD) is an estimate of the daily exposure to an agent over a full lifetime that is "likely to be without an appreciable risk of deleterious effects" for the human population, including sensitive subgroups.[FN13: EPA Integrated Risk Information System (IRIS) Glossary of terms. http://www.epa.gov/ncea/iris/help_gloss.htm#r] The RfD is not an enforceable regulatory standard; it can be used with exposure information to set clean up levels. In 2005, the National Research Council (NRC) of the National Academies of Science recommended an RfD for daily intake of perchlorate that it considered to be an acceptable level of exposure of 0.7 ug/kg/day.[FN14: NRC. 2005. Health Implications of Perchlorate Ingestion. National Research Council of the National Academies. National Academies Press, Washington, D.C.] EPA adopted this RfD and posted on its public database, the Integrated Risk Information System (IRIS) in February 2005.[FN15: EPA IRIS assessment of perchlorate. http://www.epa.gov/NCEA/iris/subst/1007.htm] While IRIS values are not regulations per se, they are used by both state and federal regulators and by the international community for a range of environmental health regulation and management purposes. For example, the information can be used in combination with exposure data to set cleanup levels at hazardous waste sites, or to set exposure standards for air, water, soil, and food. Thus, the accuracy, credibility, and timeliness of IRIS assessments have real world consequences for human health.

In simple terms, the HRL is the maximum contamination level of perchlorate that could be in drinking water, and still keep daily human consumption levels from exceeding the RfD of 0.7 ug/kg/day. It is not an enforceable standard. EPA reports that for pregnant women, exposure to perchlorate from food is 0.263 ug/kg/day at the 90th percentile (based on data from a national food survey), representing nearly 38% of the RfD, thus leaving an RSC (Relative Source Contribution) for water of 62%.[FN16: 73 Fed Reg at 60276] This is equivalent to 0.437 ug/kg/day from water, assuming an average body weight of 70 kg, and a daily water consumption of 2 L (90th percentile adult water consumption). That is, 0.437 ug x 70 kg body wt. = 30.6 ug perchlorate in 2 liters (the daily consumption amount). This is 15 ug/L, or 15 ppb, the originally proposed HRL.

The RfD for perchlorate and perchlorate salts of 0.7 ug/kg body weight/day is based on a human volunteer study, Greer et al, 2002.[FN17: Greer, M.A., Goodman, G., Pleuss, R.C., Greer, S.E. 2002. Health effect assessment for environmental perchlorate contamination: The dose response for inhibition of thyroidal radioiodide uptake in humans. Environ. Health Perspect. 110:927-937. Docket HQ- OW-2009-0297 NRDC supplemental comments on perchlorate] The RfD is for oral exposure, including food and water, and is based on radioactive iodide uptake inhibition (RAIU) in the thyroid as the critical effect. The IRIS assessment of perchlorate explains that "The point of departure is based on a non- statistically significant mean 1.8% (standard error of the mean 8.3%) decline in RAIU in healthy adults following two weeks exposure to a daily perchlorate dose of 0.7 ug/kg/day. An intraspecies uncertainty factor of 10 is applied to protect the most sensitive population, the fetuses of pregnant women who might have hypothyroidism or iodide deficiency. Dose is given as perchlorate anion."[FN18: EPA. IRIS database. Perchlorate and perchlorate salts. http://www.epa.gov/ncea/iris/subst/1007.htm#revhis]

The RfD adopted by EPA has been widely criticized as inadequately protective by state scientific experts[FN19: Ginsberg G and D Rice. The NAS perchlorate review: questions remain about the perchlorate RfD. Environ Health Perspect. 2005 Sept; 113(9):1117-9. Erratum in: Environ Health Perspect. 2005 Nov; 113(11):A732.] and by EPA's own Children's Health Protection Advisory

Committee,[FN20: Letter from Melanie Marty to Administrator Johnson regarding Preliminary Regulatory Determination on Perchlorate (November 3, 2008, PDF) http://yosemite.epa.gov/ochp/ochpweb.nsf/content/perchlorateletter.htm/$file/PerchlorateLetter.pdf] and no longer reflects the best available data.[FN21: EN Pearce, AM. Leung, BC Blount, HR Bazrafshan, X He, S Pino, L Valentin-Blasini, and LE Braverman, 2007. Breast milk iodine and perchlorate concentrations in lactating Boston-area women. J Clin Endocrinol Metab. 92(5):1673-7.] [FN22: Letter from Melanie Marty to Administrator Johnson regarding Preliminary Regulatory Determination on Perchlorate (November 3, 2008, PDF) http://yosemite.epa.gov/ochp/ochpweb.nsf/content/perchlorateletter.htm/$file/PerchlorateLetter.pdf]

Response: Please see the response to comment ID 28818 under comment code 2100.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0227
EPA Comment ID: 28818
EPA Comment Code: 2100

Comment: Acronyms: BAF: Background Adjusting Factor BW: Body weight of an adult (70Kg) DW: Drinking-Water DWL: Daily Drinking-Water Consumption in litres (2 l) GREER_NOEL: Greer 2002 NOEL(7ug/kg -day) NAS: National Academy of Sciences NOEL: Non Adverse Effect Level MCL: Maximum Contaminant Level OIG: EPA's Office of Inspection General PEC: Perchlorate Equivalent Concentration PEC-NOEL: Perchlorate Equivalent Concentration NOEL PEC-PHG : Perchlorate Equivalent Concentration PHG PHG: Public Health Goal RfD: Reference dose RSC: Relative Source Contribution SPEC: Serum Perchlorate Equivalent Concentration RAIU: Radioactive Iodine Uptake TGL: Total Urinary Goitrogen Load expressed in PEC: [Perchlorate] + [nitrate/150] + [thiocyanate/8.8] TH: thyroid Hormone UF: Uncertainty Factor UPEC: Urinary Perchlorate Equivalent Concentration

Executive Summary

In evaluating the risks posed by perchlorate and the value of regulation through establishment of an MCL, EPA is relying on information derived from a flawed analysis of the impacts of perchlorate exposure. There are two primary factors that have significantly impacted the perchlorate risk assessment, and could explain the omissions and contradictions mentioned further below.

First, the NOEL (Non Observed Effect Level) found in the Greer 2002 study from which the perchlorate RfD is derived, did not take into account existing background effect. The root of this omission could lie in the fact that a qualitative observational study, which takes into account background levels and is by far the most common human epidemiological study used in evaluating exposure risks to humans, was not performed or relied on in analyzing the impact of perchlorate in this instance. Instead, the Greer study was an experimental study on humans, which did not take into account background effects and thus significantly overstates the impact of perchlorate on human health. Therefore, the NOEL found by the Greer study is not accurate, and should not be relied upon to either regulate perchlorate or establish an RfD.

Response: EPA respectfully disagrees with the commenter. The RfD, which is derived from the NOEL, is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population that is likely to be without an appreciable risk of deleterious effects during a lifetime. The RfD, based on the assumption that thresholds exist for certain toxic effects of chemicals, represents the drinking water perchlorate exposure plus an incremental additional exposure of perchlorate from either water or food which could trigger iodine uptake inhibition, with a 10X safety factor applied. The NRC recommended that data from the Greer et al. (2002) human clinical study be used as the basis for deriving a perchlorate reference dose (RfD) (NRC 2005), and also noted that the results of this study were supported by those of other human studies. From this Greer et al. (2002) human clinical study, the statistical no observed effect level (NOEL) for the perchlorate-induced inhibition of thyroid iodide uptake was determined to be 7.0 ug/kg (a corresponding iodide uptake inhibition of 1.8%). The NRC concluded that the most health protective and scientifically valid approach to deriving a reference dose for perchlorate was to base the perchlorate RfD on the precursor event of inhibition of iodide uptake by the thyroid, which would precede any more severe adverse health effects of perchlorate exposure in humans. In this case, the NRC used a precursor to adverse thyroid effects to establish a level at which no adverse effects would be anticipated in exposed populations. This approach is consistent with the Agency's policy on the use of precursor events when appropriate in establishing the critical effect upon which an RfD is based (U.S. EPA, 2002). The NRC recommended that EPA apply an uncertainty factor of 10 to this NOEL of 7.0 ug/kg for the perchlorate-induced inhibition of thyroid iodide uptake, to account for differences in sensitivity between healthy adults and the most sensitive sub-population (fetuses of pregnant women who might have hypothyroidism or iodide deficiency). The NRC viewed the recommended uncertainty factor of 10 as conservative and protective of health, given that the NOEL is based on a non-adverse effect (iodide uptake inhibition). NRC recommended that using a non-adverse effect that is upstream of the adverse effect represents a more conservative, health-protective approach to the risk assessment for perchlorate, noting that the purpose of the 10-fold uncertainty factor is to protect sensitive subpopulations in the face of uncertainty regarding their relative sensitivity to perchlorate exposure. EPA has adopted the NRC's recommendations in its "Integrated Risk Information System" (USEPA, 2005), resulting in an RfD of 0.7 ug/kg/day, which was derived by applying a 10-fold uncertainty factor to the NOEL of 7.0 ug/kg/day. EPA used the best available peer-reviewed science, and the Agency has determined to regulate perchlorate in drinking water. EPA will continue to evaluate scientific studies of perchlorate health effects as part of the perchlorate rulemaking process. Greer MA, Goodman G, Pleus RC, Greer SE. Environ Health Perspect. 2002 Sep;110(9):927-37. National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276pp. USEPA. 2002. A review of the reference dose and reference concentration processes. Risk Assessment Forum, Washington, DC; EPA/630/P–02/0002F. USEPA. 2005. "Integrated Risk Information System (IRIS), Perchlorate and Perchlorate Salts." February 2005.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0227
EPA Comment ID: 28820
EPA Comment Code: 2100

Comment: 1.1. Introduction

The perchlorate NAS (National Academy of Sciences) RfD (Reference Dose) of 0.7ug//kg-day is based on the Greer 2002 dose response experimental clinical study[FN1: Greer MA, Goodman G, Pleus RC, Greer SE, 2002. Health Effects Assessment for Environmental Perchlorate Contamination: The Dose Response for Inhibition of Thyroidal Radioiodine Uptake in Humans. Environ. Health Perspective, 110(9):927-937.]. However the NOEL (Non Observed Effect Level) found in the Greer experimental longitudinal study did not take into account existing background effects, and therefore the Greer NOEL is not an accurate reflection of the NOEL for perchlorate.

NAS did not add this background level to the Greer NOEL level in its evaluation of perchlorate. Similarly, EPA's OIG did not do so in its December 2008 study [FN2: Office of Inspector General Scientific Analysis of Perchlorate, Assignment No. 2008-0010, December 30, 2008.]. The consequences of this omission are significant as discussed below.

Response: Please see the response to comment ID 28818 under comment code 2100.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28896
EPA Comment Code: 2100

Comment: As a reminder, Intertox provided comments to these studies in a 2008 submission; these comments are located in the EPA docket (Intertox, 2008). Intertox also provided comments to the Draft OIG report (Intertox, 2009). Nonetheless, these studies are summarized below. EPA has also posted several additional documents to the docket that require additional context.

A. The 2009 FR Notice Docket

The EPA Docket for this Notice (Docket ID No. EPA-HQ-OW-2009-0297) includes a number of documents including a commentary that provides criticism of the NRC expert panel's conclusions on perchlorate, but does not provide new scientific data from which to base a regulatory determination (Ginsberg and Rice, 2005). To provide a transparent compendium of available information, if the Agency provides or uses any commentaries, it should consider all commentaries. For example, a response to Ginsberg and Rice (2005) was published in the same journal. This response was co-authored by the NRC perchlorate panel chair and three other members from the 18-member panel and provides point-by-point science based rebuttals to why the Ginsberg and Rice (2005) assertions are incorrect. The response authors conclude by stating that the NRC-recommended RfD "provides a wide margin of safety for all subjects of all ages" (Johnston, et al., 2005). We request that EPA add this response to the docket.

Response: EPA will continue to evaluate the best available science related to perchlorate as the Agency develops a National Primary Drinking Water Regulation for perchlorate. The Johnson, et. al., commentary has been reviewed by EPA and added to the docket. Also, see response to comment code 2100.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662

EPA Comment ID: 28901
EPA Comment Code: 2100

Comment: Greer et al. (2002)

As noted above and briefly reiterated here, the mechanism of action (MOA) of perchlorate in humans is the inhibition of iodide uptake (IUI). The MOA has been reviewed by numerous authoritative bodies (NRC, EPA, ATSDR, etc.) who have concluded that it is not adverse. Iodide uptake is mediated by the NIS in the thyroid follicular cell. Greer et al. found a level where there was no statistical change in IUI and therefore, no downstream effects were possible.

That IUI is not adverse has been well-documented by NRC, EPA, New Jersey, California, and ATSDR. Much is documented about exposures to perchlorate at environmentally relevant doses up to therapeutic doses, the amount of IUI these doses cause, and the lack of downstream effects with environmentally relevant doses. For example, many studies demonstrate a statistically significant IUI, but no change in thyroid hormones for weeks or months (Greer et al., 2002; Braverman et al., 2005; Lawrence et al., 2000 and 2001; etc.). Moreover, the literature regarding perchlorate at therapeutic doses demonstrates the effect of IUI and changes in hormones. The NRC committee members unanimously stated that transient changes in thyroid hormones are not adverse and prolonged changes in thyroid hormones must occur for a person to become hypothyroid.

Some have argued that the study population of the Greer Study was too small to exhibit statistical significance of small changes in IUI particularly with the variability reported. It is important to note that decisions regarding statistical power and sample size were conducted a priori, in accordance with standard experimental design. These were stated and agreed upon by the researchers and EPA. The questions by some about variability have been raised a posteriori, after the results are known. Based on all the information available when the experiment was designed, the sample sizes in the Greer Study were sufficient. Notably, with a dose of 0.02 mg/kg-d, a 16% IUI (24-hr value) was statistically significant.

Regarding the variability of the low dose group, IUI from "background" (as noted above in Figure 3) perchlorate, nitrate, thiocyanate, and other agents found in the diet and drinking water were not controlled. This likely explains a significant proportion of daily interpersonal RAIU changes. Furthermore, 1) variability in RAIU for the low dose group was not different from RAIU for other dose groups, 2) all volunteers had normal baseline RAIU values when compared to the literature, and 3) when baseline RAIU is low, small absolute changes will appear large as relative RAIU, which is a mathematical, not physiologic, phenomenon.

In a dose-response study, one dose group should not be taken in isolation. The best way to evaluate the low-dose variability in RAIU is to examine all data generated by the study. Simple inspection of the data show a decrease in RAIU change with increasing dose-IUI occurred in a classic and unequivocal dose- response manner. Additionally, the No Effect Level (NEL) using linear regression of all relevant RAIU clinical data was 6 ug/kg-d for 24 hours, which was similar the NOEL of 7 ug/kg-d. Considering the data from Lawrence et al. (2001) which demonstrated a higher dose of perchlorate (approximately 40 ug/kg-d assuming 3 mg/d for a 70 kg person) with a non-statistically significant decrease in RAIU (as well as no corresponding change in thyroid hormones) strengthens this understanding.

Response: See response to comment code 2100. EPA will continue to evaluate all of the available science related to perchlorate as the Agency develops a National Primary Drinking Water Regulation for perchlorate.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group (EWG)
EPA Document ID: EPA-HQ-OW-2009-0297-0499
EPA Comment ID: 28936
EPA Comment Code: 2100

Comment: EWG urges the agency to take the results from this CDC study into account and revise the current RfD to reflect these findings. In written responses to questions for the record from the House Committee on Energy and Commerce dated from 2007 (attached), Dr. James Pirkle, Deputy Director for Science at the National Center for Environmental Health and coauthor of the study, had the following comments regarding the study results: "We do not think confirmatory analysis is necessary to validate Blount's analysis of the NHANES data. Although we understand that conclusions of causality can rarely be drawn based upon a single study, when viewed within the context of the available clinical literature, the findings of the Blount study are consistent with causality" (Attached). In addition, an independent analysis of the NHANES data by scientists who work for California's Office of Environmental Health Hazard Assessment confirmed CDC's findings (Steinmaus et al 2007). Given the issues with the data in the Greer study and the strengths of the Blount study, the agency should place greater weight on the results from the Blount study in its determination.

Response: In the October 10, 2008 FR Notice requesting public comments on its preliminary determination not to regulate perchlorate in drinking water (FR Vol. 73, No. 198, p. 60266), EPA considered and discusses the results of the Greer et al. (2002), and Blount et al. (2006, 2007) studies, in the process of evaluating the adverse health effects of perchlorate. Blount et al., (2006) published a study in the journal "Environmental Health Perspectives" examining the relationship between urinary levels of perchlorate and blood serum levels of TSH and total T4 in 2,299 men and women (ages 12 years and older) who participated in CDC's 2001–2002 NHANES. Blount et al. (2006) evaluated perchlorate along with a number of covariates known or likely to be associated with thyroid hormone levels, to assess the relationship between perchlorate and these hormones. The Blount et al. (2006) study found that perchlorate exposure was a statistically significant predictor of thyroid hormones in women, but not in men. For women with urinary iodide levels less than 100 ug/L, the researchers found that urinary perchlorate was associated with a decrease in T4 levels and an increase in TSH levels. For women with urinary iodide levels greater than or equal to 100 ug/L, the researchers found that perchlorate was a significant positive predictor of TSH, but not a predictor of T4. Their observations that adverse thyroid hormone effects were found in women whose urinary iodine was below 100 ug/L is suggestive of a partial study population iodine deficiency status. Blount et al. (2006) noted several limitations of their study and recommended that their findings be affirmed in other large studies focusing on women with low urine iodide levels. Since their study was cross-sectional in design, it also cannot be concluded whether or not the association between perchlorate and thyroid hormone levels is causal, or is mediated by some other correlate of both, although the relationship between urine perchlorate and total TSH and T4 levels persisted after statistical adjustments for some additional covariates known to predict thyroid hormone levels. EPA has evaluated this data as part of the regulatory determination EPA will

continue to evaluate new scientific information on the health effects of perchlorate as the Agency develops the proposed perchlorate drinking water regulation.

Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environ Health Perspect. 2006 Dec;114(12):1865-71.

Blount BC, Valentin-Blasini L, Osterloh JD, Mauldin JP, Pirkle JL. Perchlorate exposure of the US Population, 2001-2002. J Expo Sci Environ Epidemiol. 2007 Jul;17(4):400-7. Epub 2006 Oct 18.

Greer MA, Goodman G, Pleus RC, Greer SE. Health effects assessment for environmental perchlorate contamination: the dose response for inhibition of thyroidal radioiodine uptake in humans. Environ Health Perspect. 2002 Sep;110(9):927-37. Erratum in: Environ Health Perspect. 2005 Nov;113(11):A732.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 29079
EPA Comment Code: 2100

Comment: EPA's preliminary determination includes imprecise language that bears clarification:

Perchlorate interacts with the sodium iodide symporter, reducing iodine uptake into the thyroid gland and, at sufficiently high doses, the amount of T4 produced and available for release into circulation. Sustained changes in thyroid hormone secretion can result in hypothyroidism. (p. 60275; emphasis added)

[Text Box: The NAS concluded that perchlorate will not cause adverse effects under consideration in this determination. The NAS findings are consistent, as well as the overwhelming majority of the large body of available peer-reviewed science on perchlorate.]

The "sufficiently high doses" that EPA refers to are orders of magnitude higher, approximately 0.4 mg/kg-d (approximately 19,000 ppb)[FN2: See, NAS, at 171-172 (pdf version) ("...a sustained exposure at more than 0.4 mg/kg per day would most likely be required to cause a sufficience decline in iodide uptake and thyroid hormone production to result in adverse health effects in normal adults. That estimate is based on clinical studies and studies of long-term treatment of patients who had hyperthyroidism.]. These levels have never been reported in public drinking water systems. According to the NAS report, even these levels do not inevitably lead to adverse effects.

The NAS independently evaluated the science and its conclusions and recommendations are published in the report Health Implications of Perchlorate Ingestion (2005). The NAS report recommended an RfD of 0.7 ug/kg-d based on a No Observed Effect Level (NOEL), or the dose at which no effects occur, adverse or otherwise (NAS, 2005). One of the critical studies that served as the basis for this RfD was the study by Greer et al. (2002) which demonstrated that there was no inhibition of iodide uptake by the thyroid at a dose of 7 ug/kg-d. Some have argued that the low dose group contained only seven subjects; however the NAS correctly dismissed this assertion, pointing out that there were four doses provided across 37 subjects. Importantly, the NAS also

noted that it did not examine Greer in isolation. According to the NAS report, the findings in Greer are supported by other clinical studies, occupational and environmental epidemiologic studies, and studies of long-term perchlorate administration to patients with hyperthyroidism.

Further, the NAS states with emphasis,

"Inhibition of iodide uptake by the thyroid clearly is not an adverse effect; however if it does not occur, there is no progression to adverse health effects." The committee views its recommendation to use [IUI] by the thyroid as the basis of the perchlorate risk assessment to be the most health-protective and scientifically valid approach (NAS, 2005).

In using a NOEL, the NAS committee adopted a notably conservative, health- protective approach. This dose is already lower than any dose in which adverse effects occur; an additional safety factor of 10 is applied to the already conservative NOEL. The NAS was acting to ensure protection for the most sensitive individuals in a population, in this case, hypothyroid or iodine- deficient pregnant women and their developing fetuses. Importantly, the NAS panel did consider other sensitive populations besides pregnant women and their fetuses. They also considered the potential effect on infants, developing children, people who have compromised thyroid function, and people who are iodide-deficient. The NAS panel stated that using a NOEL as the point of departure is a more conservative and health-protective approach than EPA's customary approach of using the adverse effect (NAS, 2005).

The NAS panel also took time to distinguish between a No Observable Adverse Effect Level (NOAEL) from a NOEL. The experts observed that there was confusion between the two and clarified that the NOAEL is based upon an adverse effect, whereas the NOEL is based upon a dose at which no effect occurs, adverse or otherwise. (NAS, 2005).

EPA adopted the RfD recommended by the NAS and confirmed that it was conservatively based on the NOEL, not the NOAEL. EPA should clarify its finding as to the potential adverse effects of perchlorate to bring the final determination into alignment with its own NAS-based reference dose.

In sum: perchlorate will not cause adverse effects at levels under consideration in this determination. This conclusion reflects the best available scientific findings, including the NAS report and the overwhelming majority of the large body of available peer-reviewed science on perchlorate.

Response: Please see the response to comment ID 21094 under comment code 2100.

EPA Comment Code: 2110 Regulatory determination based upon the already-established RfD

Individual Comments

Commenter Name: Michael Dourson
Commenter Organization: Toxicology Excellence for Risk Assessment (TERA)
EPA Document ID: EPA-HQ-OW-2009-0297-0637
EPA Comment ID: 28493
EPA Comment Code: 2110

Comment: Our primary concerns relate to the current EPA RfD of 0.0007 mg/kg-day found on EPA's Integrated Risk Information System (IRIS), since new data have shown this value to be out of date.

Concern: EPA acknowledges in its Federal Register notice that critically important data on pregnant women and their offspring have become available since the time of the development of the EPA RfD in 2005 (EPA, 2008), but then fails to cite a prospective epidemiology study by Tellez et al. (2005) that analyzed the results of differing perchlorate exposures in pregnant mothers and their newborns. As a basis of an RfD, Tellez et al. (2005) is superior to the study used as the basis of the current RfD, that is Greer et al. (2002), since the Tellez et al. (2005) study is on the sensitive populations of interest (pregnant women and their babies). As a basis of an RfD, Tellez et al. (2005) is vastly superior to the ecological epidemiology study of Blount et al. (2006, 2007), since Tellez et al. (2005) measured perchlorate exposure in the individuals on which the effects of concern were monitored.

Recommendation: EPA needs to reconsideration its existing RfD on the basis of the Tellez et al. (2005) epidemiology study in pregnant women and their babies. This reconsideration is consistent with recommendations of the NAS (2005) on page 69 of its report.

Concern: NAS (2005, pages 9 and 112) admits that it did not follow EPA's traditional RfD method when it developed their value. Since EPA adopted the NAS RfD, the inescapable conclusion is that EPA did not follow it own RfD method either. More importantly, lack of adherence to EPA's methods will encourage others to do so as well, resulting in a potpourri of values with little resemblance to those that already exist on EPA's Integrated Risk Information System (IRIS) or elsewhere.

Recommendation: Recalculate the existing perchlorate RfD using EPA's published methods.

See the attached file for details. Reviewed using developmental reserve. [See PDF Docket ID EPA-HQ-OW-2009-0297-0637; Note that this attachment is identical to Docket ID EPA-HQ-OW-2008-0692-1562; responses to this comment are provided through Docket ID EPA-HQ-OW-2008-0692-1562.]

Response: See response to comment ID 28863 under comment code 2110.

EPA will consider the best available peer reviewed data in developing an NPDWR for perchlorate, including the data from the Tellez study.

Commenter Name: Jonathan Borak
Commenter Organization: Yale School of Medicine
EPA Document ID: EPA-HQ-OW-2009-0297-0209
EPA Comment ID: 28506
EPA Comment Code: 2110

Comment: My submitted comments are contained in the attachment. Thank you for this opportunity to contribute to the Agency's efforts.

Jonathan Borak, MD, DABT, FACP, FACOEM

Attachment

September 16, 2009

Water Docket Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Avenue, NW Washington, DC 20460

Re: Docket ID No. EPA-HQ-OW-2009-0297

Dear Sir or Madam:

At the request of the Perchlorate Study Group, I am writing as a physician and toxicologist in response to your request for comments (Fed Reg 74:41883, 08/19/09) regarding EPA's perchlorate regulatory determination. By way of introduction, I am Clinical Professor of Epidemiology and Medicine at Yale School of Medicine, Director of the Yale University Interdisciplinary Risk Assessment Forum, and a faculty member of the Yale Occupational and Environmental Medicine Program. I serve as Co-Chair of the Council on Scientific Affairs of the American College of Occupational and Environmental Medicine (ACOEM), was Editor and Course Director of the ACOEM Core Curriculum in Environmental Medicine, and served as a founding member of EPA's National Advisory Committee to Develop Acute Exposure Guideline Levels for Hazardous Substances.

1.) First and foremost, I support the Agency's decision to base its regulatory decision upon the current RfD, and not upon the findings of studies published since 2005 (Fed Reg 74:41892, 08/19/09). Over the past several years, much attention has been given to findings reported by Blount et al. (1), who analyzed data from the CDC's 2001-2002 NHANES study and performed additional analyses on NHANES urine samples.

Response: The Agency believes that the current RfD is appropriate for purposes of this regulatory determination.

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638

EPA Comment ID: 28745
EPA Comment Code: 2110

Comment: 2. The findings of several studies conducted since 2005 suggest that the EPA- adopted reference dose of 0.7 ug/kg-day is a conservative and health-protective reference dose that has a 10-fold uncertainty factor applied to the point of departure to account for differences between healthy adults and the most sensitive population: fetuses of pregnant women who might have hypothyroidism or iodide deficiency. Consequently, additional non-standard adjustments appear unnecessary because the health of the most sensitive sub-population (fetuses and neonates) has already been considered. Application of an appropriately calculated relative source contribution (RSC) term, as was conducted during development of the December 2008 Health Advisory (HA), appears adequate and appropriate.

Response: EPA believes that the RfD indicated by the NAS is appropriate. EPA has not yet determined how best to develop the MCLG for perchlorate. EPA plans to seek comments on its development of its proposed regulation, including the MCLG, as required by the SDWA.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection (MassDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0495
EPA Comment ID: 28863
EPA Comment Code: 2110

Comment: 5) Although the HRL of 2 ppb recommended above is numerically similar to the maximum contaminant level adopted by MassDEP and protective of the sensitive segment of the population, the RfDs used by the two agencies as the bases to derive the drinking water levels are different. MassDEP concluded that the National Research Council's (NRC) RfD is not protective of public health (Zewdie et al. 2009). Although uncertain, the EPA's modified PBPK analysis presented in Table 1 for a 7-day-old healthy infant supports this position. In this analysis, the infant gets about 3 times the maternal dose through breast milk at the dose equal to the point-of-departure (POD) in the NRC RfD derivation. This translates to a 7-day infant receiving about 20 ug/kg/day (0.02 mg/kg/d) dose of perchlorate through breast milk from a mother ingesting 7 ug/kg/day. This dose level is equivalent to the exposure level that resulted in significant inhibition (17 %) of iodide uptake in healthy adults in the Greer et al. (2002) study, suggesting that the factor of 10 applied to the POD by the NRC to protect sensitive individuals is insufficient. An additional uncertainty factor is required to extrapolate from LOAEL to NOAEL as 0.02 mg/kg/day is an effect level. Efforts to determine populations at risk based on the NRC RfD will yield significant underestimates of those at risk. MassDEP can support EPA's decision to not re-evaluate the NRC RfD at this time, if EPA adopts an HRL of 2 ppb or lower.

Response: With regards to conclusions of the NRC panel on the effects of perchlorate exposure, EPA believes the NRC appropriately based the RfD on iodide uptake inhibition to the thyroid, for the reasons discussed in its report. The NRC (2005) identified "the fetus of pregnant women who might have hypothyroidism or iodide deficiency" as "the most sensitive population," but also identified infants and developing children as additional "sensitive populations." Infants and young children have greater exposure to contaminants in food and water because of greater consumption of food and water on a per unit body weight basis. Therefore, these life stages may be the most vulnerable populations when their relative exposure is considered. EPA believes that infants may be

most exposed and have a greater potential for exceeding the RfD because of body weight and consumption. It is important to consider that the source of the perchlorate in breast milk is probably due to a much greater extent to the greater prevalence of perchlorate in food, than due to comparatively lesser prevalence of perchlorate in drinking water. The NRC recommended that EPA apply an uncertainty factor of 10 to the NOEL of 7.0 ug/kg for the perchlorate-induced inhibition of thyroid iodide uptake, to account for differences in sensitivity between healthy adults and the most sensitive sub-population, consisting of fetuses of pregnant women who might have hypothyroidism or iodide deficiency. Iodide uptake inhibition has been identified in the literature as an area of concern in connection with increasing the risk of neurodevelopmental impairment in fetuses of high-risk mothers. The NRC viewed the recommended uncertainty factor of 10 as conservative and protective of health, given that the NOEL is based on a non-adverse effect (iodide uptake inhibition) which precedes the adverse effect in a continuum of possible adverse biological effects of perchlorate exposure. NRC recommended that using a non-adverse effect that is upstream of the adverse effect represents a more conservative, health-protective approach to the risk assessment for perchlorate, noting that the purpose of the 10-fold uncertainty factor is to protect sensitive subpopulations in the face of uncertainty regarding their relative sensitivity to perchlorate exposure. EPA has adopted the NRC's recommendations in its "Integrated Risk Information System" (IRIS) (USEPA 2005), resulting in an RfD of 0.7 ug/kg/day, which was derived by applying a 10-fold (10x) uncertainty factor to the NOEL of 7.0 ug/kg/day. EPA used the best available peer-reviewed science, and the Agency has determined to regulate perchlorate in drinking water. EPA will be reevaluating this issue as part of the perchlorate rulemaking. Greer MA, Goodman G, Pleus RC, Greer SE. Health effects assessment for environmental perchlorate contamination: the dose response for inhibition of thyroidal radioiodine uptake in humans. Environ Health Perspect. 2002 Sep;110(9):927-37. Erratum in: Environ Health Perspect. 2005 Nov;113(11):A732. National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276pp. USEPA. 2005. "Integrated Risk Information System (IRIS), Perchlorate and Perchlorate Salts." February 2005. Available on the Internet at: http:// www.epa.gov/iris/subst/1007.htm.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28895
EPA Comment Code: 2110

Comment: III. OTHER COMMENTS

In Section IV of the Notice, EPA discusses its consideration of studies published since EPA adopted the NRC RfD for perchlorate. The Notice states:

EPA's preliminary regulatory determination is based on NRC's (NRC, 2005) recommendation to use data from the Greer et al. (2002) study as the basis for the perchlorate RfD/risk assessment. Since the publication of the NRC report, researchers have investigated perchlorate occurrence in humans by analyzing for perchlorate in urine and breast milk-such biomonitoring data has the potential to better inform EPA's analysis of exposure to perchlorate through food and water and to provide insight into the possible interactions of other physiologic conditions (e.g., iodine deficiency) with perchlorate ingestion. EPA's preliminary regulatory determination described the consideration of

these studies, many of which were published after the NRC report (including, but not limited to, Blount et al. (2006 and 2007), Steinmaus et al. (2007), and Amitai et al. (2007)).

EPA's conclusion to this section is:

EPA agrees that additional important data have become available since the RfD was derived in 2005. However, EPA has evaluated the new data and has decided to make the regulatory determination based upon the current RfD.

The weight-of-scientific evidence supports this EPA conclusion.

Response: EPA believes that the RfD indicated by the NRC is appropriate. As discussed in this FR notice, EPA has decided the model does not directly bear on the current decision regarding the need for a NPDWR for perchlorate. EPA is continuing to evaluate whether the model could be used in setting a NPDWR for perchlorate.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group (EWG)
EPA Document ID: EPA-HQ-OW-2009-0297-0499
EPA Comment ID: 28927
EPA Comment Code: 2110

Comment: - EPA must modify the RfD that is the basis for its standard setting to include a substantial body of peer-reviewed science published since 2002, including two large, high quality epidemiologic studies from the CDC (Blount et al 2006a, Blount et al 2006b). In addition to these new studies, peer reviewed analyses of the study that forms the basis for the current RfD (Greer 2002) have revealed fatal flaws with this work. A study with such fundamental and well-documented shortcomings cannot be used as the basis to determine national safety standards for exposure to this potent thyroid toxin.

Response: See response to comment ID 28863 under comment code 2110.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 29077
EPA Comment Code: 2110

Comment: EPA is justified in making a regulatory determination based upon the current Reference Dose (RfD), which includes a 10-fold uncertainty factor (UF) to account for sensitive life stages; further reductions for sensitive life stages are duplicative and not scientifically justified. Importantly, authoritative bodies concur that the RfD is based on a No Observed Effect Level (NOEL), which is a more conservative approach than EPA's traditional use of a No Observed Adverse Effect Level (NOAEL). In establishing the threshold for IUI-which is defined by the National Academy of Sciences as a nonadverse effect-as the point of departure, EPA has already ensured that downstream adverse effects due to perchlorate (which to date have not been reported in humans exposed to perchlorate at environmental levels) will not occur (NRC, 2005). Since much information regarding

the perchlorate mechanism of action is known, EPA should use PBPK modeling based on the best science rather than the estimations in the alternative HRL calculations.

Response: EPA believes that the RfD indicated by the NRC is appropriate. As discussed in this FR notice, EPA has decided the model does not directly bear on the current decision regarding the need for a NPDWR for perchlorate. EPA is continuing to evaluate whether the model could be used in setting a NPDWR for perchlorate.

EPA Comment Code: 2150 EPA's decision not to seek further input from the NRC on issues related to perchlorate

Response to Comment Code 2150: On October 10, 2008, EPA published a Federal Register notice presenting the Agency's preliminary regulatory determination for perchlorate and supporting rational for this determination, in accordance with the Safe Drinking Water Act (SDWA) (Federal Register Vol. 73, No. 198, p. 60262). In this October 10, 2008 Federal Register notice, EPA determined that a national primary drinking water regulation (NPDWR) for perchlorate would not present a meaningful opportunity for health risk reduction for persons served by public water systems. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, the opportunity for health risk reduction through a national primary drinking water standard, and also requested comment on whether further review by the NRC would be warranted. In January of 2009, EPA announced that the Agency planned to seek additional input from the National Research Council (NRC) on perchlorate. The NRC previously studied perchlorate health implications from March, 2003 until they issued their report in January, 2005 (NRC 2005). EPA has compiled and evaluated additional scientific studies relevant to perchlorate health effects and exposure available in the scientific literature since publication of the 2005 NRC report. EPA also has obtained peer review and public comment on the Agency's analysis of a number of these studies. The Agency currently believes that further review by the NRC would unnecessarily delay regulatory decision making for perchlorate. EPA also notes in this August 19, 2009 Federal Register notice that if the Agency were to make a final determination to regulate perchlorate, the Agency, in accordance with the SDWA, would seek review by the Science Advisory Board prior to proposal of any maximum contaminant level goal and national primary drinking water rule. Therefore, EPA is not, at present, planning to request additional NRC review of issues related to perchlorate.

Individual Comments

Commenter Name: Julie L. Heckman
Commenter Organization: American Pyrotechnics Association (APA)
EPA Document ID: EPA-HQ-OW-2009-0297-0522
EPA Comment ID: 28492
EPA Comment Code: 2150

Comment: EPA's Commitment to Use Sound Science

In January of this year, EPA announced that it would reevaluate the science regarding perchlorate's potential health effects, with particular emphasis on evaluating the effects of perchlorate exposure on infants and young children. The Agency further announced that it planned to seek additional advice from the National Research Council ("NRC") on perchlorate before making a final determination. Since the time NRC last issued its January 2005 report on perchlorate,[FN1: National Research Council, Health Implications of Perchlorate Ingestion, National Academies Press, Board on Environmental Studies and Toxicology (January 2005). Subsequently in 2005, EPA adopted the

NRC recommended reference dose of 0.0007 mg/kg per day, which translates to a drinking water equivalent level of 24.5 ppb ("DWEL"). In January 2006 EPA's Superfund office issued guidance adopting the NRC reference dose and DWEL of 24.5 ppb as the recommended value to be considered as the preliminary remediation goal to guide perchlorate assessment and cleanup at Superfund sites. In January 2007, EPA reported that it had collected sufficient occurrence data, and that further monitoring was not needed for the Agency to make a regulatory determination. 72 Fed. Reg. 367 (January 4, 2007). In October of 2008, EPA announced a preliminary determination not to regulate perchlorate, noting that less than 1% of water systems have perchlorate levels above the health reference level. EPA concluded that perchlorate failed to meet two regulatory criteria (i.e., that a contaminant occur frequently at levels of health concern, and that establishing a national drinking water standard would provide a "meaningful opportunity for health risk reduction"). Then, in January 2009, EPA announced that it was replacing the perchlorate preliminary remediation goal of 24.5 ppb with an interim health advisory, establishing a nonenforceable concentration of contaminants in drinking water at which no adverse health effects are expected to occur, of 15 ppb. In the face of this uncertainty and regulatory history, debate over the science of perchlorate health risks has continued.] EPA has compiled and evaluated additional scientific studies relevant to perchlorate health effects and exposure that were not available to the NRC. However, in its August 19, 2009 Notice, EPA announced that it would, in fact, not seek further review by the NRC because it believed such review would "unnecessarily delay" regulatory decision making for perchlorate.

Concerns about protection of human health and the environment must always be in the fore front of our thinking, but to do so properly, sound science should not be sacrificed in the interest of mere expediency. The APA firmly believes that EPA should ask the NRC to review the new information to assist EPA with its determination. EPA has spent years assessing perchlorate's health effects and occurrence to determine whether a national standard is warranted.[FN2: Under the Safe Drinking Water Act ("SDWA"), [Sec] 1412, to regulate a contaminant in drinking water, EPA must determine that it meets three criteria: (1) The contaminant may have an adverse effect on human health, (2) the contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern, and (3) regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems. These legal criteria are premised on the use and application of sound science.] In the interest of obtaining the best available scientific information and advice, a comprehensive NRC review should be preferred.[FN3: The Notice specifically requested comment upon whether further review by the NRC is warranted, 74 Fed. Reg. 41884, and noted that if the Agency were to make a final decision to regulate perchlorate, it would seek review by the Science Advisory Board ("SAB") prior to proposal of any maximum contaminant level goal and national primary drinking water rule. Id. However, the statutorily required review by the SAB under section 1412 of the SDWA to comment prior to setting the levels of a maximum contaminant level goal and national primary drinking water regulation, should not be a substitute for the timely scientific review of the NRC prior to the Agency's predicate decision making responsibility under the SDWA on whether regulation is warranted in the first place. Rigorous application of scientific review and sound science principles, especially by outside independent entities, should inform each statutorily- required regulatory step and decision, not only the final one. Indeed, it is the first step that has been the most controversial and it is that process of reevaluation in which the Agency is currently engaged.]

EPA has, itself, recognized the significant scientific complexity involved here. "The public comments EPA received pursuant to the October 10, 2008, notice of preliminary regulatory determination and from the peer review of the supporting documents underscore the complexity of

the scientific issues regarding the regulatory determination for perchlorate in drinking water." 74 Fed. Reg. 41884. Given that complexity, thorough review, analysis, and input from all available sources, including the NRC, should be sought to ensure full Agency consideration of the latest and best available science and thinking.

EPA's website addressing "Using Sound Science" reiterates the importance of thorough scientific review:

We depend upon sound science to do our work. Scientific information is especially important in the development of regulations. Whether we are developing a standard to protect the public from a newly recognized risk or defining monitoring requirements to gauge how well an environmental control is working, we incorporate the most current and credible scientific information into our regulation development process. . . . EPA relies, to the extent possible, on information that has undergone thorough peer review. During peer review, qualified, independent experts provide critical assessments to ensure that activities are technically supportable, competently performed, properly documented, and consistent with established quality criteria.... We also regularly solicit outside expertise from the National Research Council, other federal agencies with related responsibilities, and other scientific organizations.[FN4: Using Sound Science, available at: http://www.epa.gov/lawsregs/brochure/science.html]

This Administration has reaffirmed the federal government's commitment to the principles of scientific integrity and the incorporation of full and open scientific review in all its policy-making functions. On March 9, 2009, the President issued his Memorandum on Scientific Integrity, directed to the heads of executive departments.[FN5: Available at: http://www.whitehouse.gov/the_press_office/Memorandum-for-the-Heads-of- Executive-Departments-and-Agencies-3-9-09/), published at 74 Fed. Reg. 10671 (March 11, 2009).] The President stated:

"science and the scientific process must inform and guide decisions of my Administration on a wide range of issues, including improvement of public health [and] protection of the environment."

He charged the Director of the Office of Science and Technology Policy with "the responsibility for ensuring the highest level of integrity in all aspects of the executive branch's involvement with scientific and technological processes." As the President further emphasized:

The public must be able to trust the science and scientific process informing public policy decisions. Political officials should not suppress or alter scientific or technological findings and conclusions. If scientific and technological information is developed and used by the Federal Government, it should ordinarily be made available to the public. To the extent permitted by law, there should be transparency in the preparation, identification, and use of scientific and technological information in policymaking.

In response to the March 9 Presidential Memorandum on Scientific Integrity, we understand that EPA's Office the Science Advisor ("OSA") has been working with the White House Office of Science and Technology Policy ("OSTP") to develop recommendations for the President and with EPA's Science Policy Council to establish the EPA position on the topic. See http://www.epa.gov/osa/scientific_integrity.htm. As the OSA has explained:

The role and use of science at EPA are determined by the nature of scientific information and how it fits within the context of Agency decision-making. Scientific information--whether it comes from EPA, other agencies, academia, the regulated community, or other sources-- always includes some degree of uncertainty and is subject to varying interpretations. For example, assessments of risks to humans from exposure to chemicals are often based on tests in which laboratory animals are given high doses of a chemical. Effects seen in the animals may or may not appear in humans, who are typically exposed to much lower doses and whose bodies may metabolize the chemicals differently. In addition, there are often different scientifically justifiable ways to conduct risk assessments, and the method chosen by the assessor can significantly impact the risk estimate.

Scientific knowledge is not only uncertain, but also dynamic. Through research that is designed to reduce uncertainties, our understanding increases and, as a result, we change our assumptions about the impacts of environmental problems and how they should be addressed....

Science does not drive EPA's policy and regulatory decisions, but rather, along with other relevant factors, informs and supports those decisions. Implementation costs and technological feasibility, local autonomy versus federal control, and justice and equity--all of which impact our quality of life and standard of living--are among the considerations that need to be factored into EPA's decisions without compromising scientific integrity, the Agency's mission, or statutory mandates. The impacts or limitations of these non-science factors, as well as the current state-of-the-science, will influence how scientific considerations are brought to bear on a particular environmental problem facing the Agency.[FN6: See http://www.epa.gov/osa/osa.htm.]

Administrator Jackson recently testified in front of the U.S. Senate Committee on Environment and Public Works on "Scientific Integrity and Transparency Reforms at the Environmental Protection Agency" on June 9, 2009,[FN7: Available at: http://www.epa.gov/ocir/hearings/.] that "[t]he public health and environmental laws that Congress has enacted depend on rigorous adherence to the best available science... While the laws that EPA implements leave room for policy judgments, the scientific findings on which of these judgments are based should be arrived at independently using well-established scientific methods, including peer review, to assure rigor, accuracy, and impartiality." In her testimony, Administrator Jackson acknowledged that, "Environmental science is complex and multi-faceted, and able scientists may not always agree on what methodologies should be employed or how studies should be interpreted. I am committed to fostering a culture of robust scientific debate and discussion within the Agency, recognizing that in the end senior scientists must take responsibility for resolving differences of opinions using established science policies and their best professional judgment."

APA respects and supports the Agency's paramount obligation to protect water quality and public health. We respectfully ask that the Agency take its own commitment to use sound science, as well as the directive of the White House to observe the highest principles of scientific-integrity, into account as it decides whether to ask the NRC or others to perform additional scientific review on the admittedly complex questions surrounding perchlorate. EPA has sought these additional comments from the public in "an effort to ensure consideration of all the potential options for evaluating whether there is a meaningful opportunity for human health risk reduction of perchlorate through a national primary drinking water rule." 74 Fed. Reg. 41883. No less so should EPA again seek the widely respected expertise, comments and advice of the NRC on this most difficult of public health issues, especially where that NRC review has proved so beneficial in the very recent

past to a full and robust consideration of the scientific data and uncertainties that must inform sound public health policy.

Because the science and policy judgments underlying your decision-making for regulating perchlorate in drinking water are extraordinarily complex and will impact not only public health but also the environment and our businesses, full consideration of all available scientific information as well as all available peer review of that information, is clearly warranted. Please reconsider your decision not to seek further review by the NRC of all the critical studies, data, and risk analyses in this important process, so that EPA may have the benefit of the most rigorous and complete analysis of the available scientific data on which to deliberate and act. To ensure that this commitment to scientific integrity be met, while EPA could simply look at the same information again and ask the public if it has any new thoughts on how to interpret that information, we would respectfully suggest EPA request, as it originally intended to do,[FN8: See Congressional Research Service, CRS Report to Congress, Perchlorate Contamination of Drinking Water: Regulatory Issues and Legislative Actions, August t, 2009, p. 5.] that the NRC study and provide to EPA an evaluation of impacts to infants and young children from perchlorate and evaluate the more recent studies, EPA's use of models, and its derivation of the 15 ppb health reference level, as well.

Thank you for your consideration of our comments and our request that the Agency take advantage of the full panoply of available means to incorporate rigorous scientific review into your process for reevaluating the risks, and the EPA's proposed additional approaches to analyzing the data, related to EPA's perchlorate determination. EPA should receive benefit of further NRC analysis of the latest data which will ensure that the Administration's commitment and mandate to use of sound science in policy- making is fulfilled.

Respectfully submitted, Julie L. Heckman Executive Director cc: Administrator Lisa Jackson Assistant Administrator for Water

Response: EPA is committed to the application of sound science and the principles of scientific integrity in its decision-making. The proposed path forward is designed to ensure adherence to both. See response to comment ID 28835 under comment code 2150.

Commenter Name: Andria Ventura
Commenter Organization: Clean Water Action et al.
EPA Document ID: EPA-HQ-OW-2009-0297-0528
EPA Comment ID: 28516
EPA Comment Code: 2150

Comment: Finally, we wish to discourage EPA from again referring the perchlorate assessment to the National Research Council (of the National Academies of Sciences) for further review. The last time (2005) the NRC reviewed perchlorate, it overstepped its charge and recommended a reference dose. This usurped EPA's authority and made it difficult for the public to comment at a key phase in the regulatory process. Furthermore, NRC committees meet a handful of times over many months. A referral would delay the process without a great deal of additional review.

Response: See response to comment code 2150 and comment ID 28822 under comment code 2150.

Commenter Name: Kathy Dolan
Commenter Organization: Food and Water Watch (FWW)
EPA Document ID: EPA-HQ-OW-2009-0297-0526
EPA Comment ID: 28609
EPA Comment Code: 2150

Comment: Your decision to not request additional NRC review of issues relating to perchlorate is ill advised. Additional NRC research may better elucidate the health effect and exposure risk we presently face. Moreover, NRC research may provide better guidance in making a final regulatory determination, especially in determining the best health reference level (HRL).

Response: See response to comment ID 28822 under comment code 2150.

Commenter Name: Apparent Mass Mailing #11 - Food and Water Watch
EPA Document ID: EPA-HQ-OW-2009-0297-0526
EPA Comment ID: 28615
EPA Comment Code: 2150

Comment: Your decision to not request additional NRC review of issues relating to perchlorate is ill advised. Additional NRC research may better elucidate the health effect and exposure risk we presently face. Moreover, NRC research may provide better guidance in making a final regulatory determination, especially in determining the best health reference level (HRL).

Response: Please see the response to comment ID 28822 under comment code 2150.

Commenter Name: Nsedu O. Witherspoon
Commenter Organization: Children's Environmental Health Network
EPA Document ID: EPA-HQ-OW-2009-0297-0674
EPA Comment ID: 28741
EPA Comment Code: 2150

Comment: Finally, we wish to discourage EPA from again referring the perchlorate assessment to the National Research Council (of the National Academies of Sciences) for further review. A referral would delay the process without a great deal of additional benefit.

Response: See response to comment code 2150 and comment ID 28822 under comment code 2150.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28797
EPA Comment Code: 2150

Comment: HISTORY OF DELAY

EPA had evidence in the 1980's that perchlorate was leaching from military dumpsites into groundwater, as documented in a 1985 interagency letter from EPA to the Centers for Disease

Control and Prevention (CDC) reporting on levels as high as 300-800 ppb "potentially affecting 32,000 to 42,000 households."[FN24: As documented in: Sass J. U.S. Department of Defense and White House working together to avoid cleanup and liability for perchlorate pollution. Int J Occup Environ Health. 2004. Jul-Sep;10(3):330-4.] EPA set a provisional RfD of 0.0001 mg/kg/day in 1992; this would have been equivalent to an MCL of 3.5 ppb in water, presuming an adult average body weight and daily water consumption, and presuming no other sources of perchlorate.[FN25: As documented in: Sass J. U.S. Department of Defense and White House working together to avoid cleanup and liability for perchlorate pollution. Int J Occup Environ Health. 2004. Jul- Sep;10(3):330-4.] It has been 17 years since that provisional RfD, and in that time the science supporting that RfD has grown significantly stronger, along with public concern and Agency interest. Moreover, the RfD now finalized is 0.7 ug/kg/day, not dramatically different from the provisional RfD 17 years ago, given the extremely lengthy delay.

EPA's progress on this assessment has been extensively and repeatedly reviewed by the interagency panel that was created in 1998 as a partnership between EPA, the U.S. Department of Defense , and other federal agencies to review perchlorate issues.

In 2002, EPA issued an External Review Draft that recommended a limit of 1 ppb in drinking water. This was sent to the NRC for review in 2004, which resulted in the recommended oral RfD of 0.0007 mg/kg/day, adopted by EPA in 2005.

REQUEST FOR COMMENT ON NRC REVIEW

NRDC Response: Further Review by NRC Not Warranted

After over 17 years of accumulated science (documented above), two EPA toxicological reviews (1998, 2002), and a lengthy NRC review (2004), it is past time for EPA to take effective regulatory action to protect people's health by preventing exposure to perchlorate. Therefore, NRDC supports the Agency's belief that further review by the NRC would create an unnecessary delay without adding anything to the scientific rigor of the Agency's determination.

NRDC would likely support the Agency if it requested a review by its Scientific Advisory Board, since it would be more rapid and less costly than an NAS review, while providing scientific oversight.

Response: See the response to comment ID 28822 under comment code 2150.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0227
EPA Comment ID: 28822
EPA Comment Code: 2150

Comment: Given these significant concerns, EPA should also move forward with its alternative proposal to seek additional input from the National Research Council of the NAS, regarding the health impacts of (synthetic and natural) perchlorate, and should specifically request input regarding the issues presented in these comments, including the problems associated with the Greer NOEL and the RfD.

Response: The NRC previously studied perchlorate health implications from March, 2003 until they issued their report in January, 2005 (NRC, 2005). EPA has compiled and evaluated additional scientific studies relevant to perchlorate health effects and exposure available in the scientific literature since publication of the 2005 NRC report. EPA also has obtained peer review and public comment on the Agency's analysis of a number of these studies. The Agency currently believes that further review by the NRC would unnecessarily delay regulatory decision making for perchlorate. EPA also notes in this August 19, 2009 Federal Register notice that if the Agency were to make a final determination to regulate perchlorate, the Agency, in accordance with the SDWA, would seek review by the Science Advisory Board prior to proposal of any maximum contaminant level goal and national primary drinking water rule. Therefore, EPA is not, at present, planning to request additional NRC review of issues related to perchlorate.

National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276pp.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28828
EPA Comment Code: 2150

Comment: Review By NAS. In the October 10, 2008 Federal Register notice (73 FR 60262) EPA stated that it would send its review of the science surrounding perchlorate again to the NAS. AMWA still believes the analysis should go to NAS for review although the association's reasons have shifted in light of the agency's new analysis of alternative HRLs. Specifically, AMWA believes a review by NAS of EPA's new analysis and methodology explained in this NODA for determining alternative HRLs is judicious because this analysis is the first time the agency has applied its 2005 Guidance. It is also prudent as EPA is asking for comment on using the PBPK model for evaluating the relative sensitivity of the various life stages to perchlorate exposure in drinking water.

AMWA recommends that EPA send both the revised PBPK model as well as the analysis used to derive alternative HRLs to NAS for review because the potential precedent that will be set if these analyses are used in rulemaking have significant ramifications for how policy is developed. Particularly where endocrine disrupting compounds are concerned, the impacts of particular chemicals on children's development must be properly characterized and modeled. Specifically, AMWA recommends that an NAS review panel be formed to address the questions posed in section A.4 of 74 FR 41886. In addition, NAS should be asked to determine the merits of the alternative approaches for calculating HRLs detailed in section B.3 (74 FR 41887-41889) and specifically with regard to EPA's request for comments in B.4 (74 FR 41889).

AMWA has additional comments related to the NAS review later in this comment letter where EPA's specific requests for comment are identified.

Response: See the response to comment ID 28822 under comment code 2150.

Commenter Name: Diane VanDe Hei

Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28834
EPA Comment Code: 2150

Comment: Part II: Specific EPA requests for comment

74 FR 41884: "EPA requests comment upon whether further review by [the National Research Council] NRC is warranted. EPA also notes that if the Agency were to make a final determination to regulate perchlorate the agency would seek review by the SAB prior to proposal of any MCLG or national primary drinking water rule."

Response: In previous comments, AMWA suggested that EPA send its review of the perchlorate science to NAS for review by 2011 (or sooner if the agency so desires). As expressed earlier in this comment letter, AMWA still believes the analysis should go to NAS for review although the association's reasons have shifted in light of the agency's new analysis of alternative HRLs.

AMWA disagrees with EPA that another review by NAS/NRC could slow the process. Previous NAS/NRC panels have finished their work in short time spans and EPA could convene a panel concurrent with the development of a perchlorate regulation, should the agency make a determination to regulate perchlorate.

EPA states in the NODA that it will have the Science Advisory Board (SAB) review any regulatory determination made prior to proposal of the regulation. This is required in Section 1412 of the SDWA and AMWA agrees that this is a good and appropriate course of action. However, a SAB review would likely focus on the entire perchlorate regulatory proposal rather than specific components of the proposal.

As a result, AMWA believes that a focused NAS/NRC review of the alternative HRL analysis that used EPA's 2005 Guidance as well as the 2008 Child-Specific Exposure Factors Handbook is necessary because of the broad potential policy implications for OGWDW and the analysis of future regulations. In addition, the mission of the NAS, in particular NRC, "is to improve government decision-making and public policy, increase public education and understanding, and promote the acquisition and dissemination of knowledge in matters involving science, engineering, technology, and health. The institution takes this charge seriously and works to inform policies and actions that have the power to improve the lives of people in the U.S. and around the world." (http://sites.nationalacademies.org/NRC/index.htm)

A NAS/NRC panel should be selected with expertise in mind to address the questions put forward in the FR notice. The new analysis to determine HRLs, as well as the agency's additional consideration for using the PBPK model, should also be peer reviewed by experts who are well versed in modeling.

Response: See the response to comment ID 28822 under comment code 2150. The SAB will consider all aspects of the NPDWR, including the scientific evaluations underlying it.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)

EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28835
EPA Comment Code: 2150

Comment: Should EPA decide not to seek review by NAS, AMWA strongly recommends that EPA include in the charge to SAB the requests for comment surrounding the alternative HRLs analysis found in this NODA (Section A. 4 of 74 FR 41886). In addition, NAS should be asked to determine the merits of the alternative approaches for calculating HRLs detailed in section B. 3 (74 FR 41887-41889) and specifically with regard to EPA's request for comments in B.4 (74 FR 41889). AMWA also strongly recommends that EPA provide at least six months for SAB to review the alternative HRL analysis and PBPK model as it relates to this analysis. EPA should also take care to ensure that there are sufficient reviewers with the proper expertise for the task.

Response: See response to comment ID 28822 under comment code 2150. EPA will ensure that the charge to the SAB and the composition of the panel are appropriate for the review of the entire scientific underpinnings of the NPDWR.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection (MassDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0495
EPA Comment ID: 28859
EPA Comment Code: 2150

Comment: Section II: Background

MassDEP supports EPA's opinion that further review by the National Research Council (NRC) will delay regulatory decision-making and supports EPA's current plan to publish alternative approaches to interpreting the data on perchlorate and to consider public comments towards making a regulatory decision on perchlorate in drinking water.

Response: EPA agrees with the commenter as discussed in the response to comment ID 28822 under comment code 2150. Also, see response to comment code 2150.

EPA Comment Code: 2200 Use of NHANES biomonitoring data for health effects evaluation

Response to Comment Code 2200: After a report prepared by the NRC (National Research Council) on "Health Implications of Perchlorate Ingestion" (NRC 2005) was released, several papers were published that investigated whether biomonitoring data associated with the National Health and Nutrition Examination Survey (NHANES) could be used to discern if there was a relationship between perchlorate levels in the body and thyroid function. Blount et al., (2007) published a study examining the relationship between urinary levels of perchlorate and blood serum levels of TSH and total T4 in 2,299 men and women (ages 12 years and older) who participated in CDC's 2001–2002 NHANES. Blount et al. (2007) evaluated perchlorate along with a number of covariates known or likely to be associated with T4 or TSH levels to assess the relationship between perchlorate and these hormones, and the influence of other factors on this relationship, including gender, age, race/ethnicity, body mass index, serum albumin, serum cotinine (a marker of nicotine exposure), estimated total caloric intake, pregnancy status, post-menopausal status, premenarche status, serum C-reactive protein, hours fasting before sample collection, urinary thiocyanate, urinary nitrate, and use of selected medications. The Blount et al. (2007) study found that perchlorate exposure was a statistically significant predictor of thyroid hormones (T4) in women with urinary iodine levels <100 ug/l, but not in men. Blount et al. (2007) noted several limitations of their study and recommended that their findings be affirmed in at least one more large study focusing on women with low urine iodide levels. Since their study was cross-sectional in design, it also cannot be concluded whether or not the association between perchlorate and thyroid hormone levels is causal, or is mediated by some other correlate of both, although the relationship between urine perchlorate and total TSH and T4 levels persisted after statistical adjustments for some additional covariates known to predict thyroid hormone levels (e.g., total kilocalorie intake, estrogen use, and serum C-reactive protein levels). An additional paper by Blount et al., (2006), found that almost all participants in the NHANES survey, including the participants in this first group, had urinary levels of perchlorate corresponding to estimated dose levels that are below the RfD of 0.7 μg/kg/day.

The Blount et al. (2006) study suggested that perchlorate could be a surrogate for another unrecognized determinant of thyroid function, since there are other chemicals, including nitrate and thiocyanate, which can affect thyroid function. Steinmaus et al., (2007) further analyzed the data from NHANES 2001–2002 to assess the impact of smoking, cotinine and thiocyanate on the relationship between urinary perchlorate and blood serum T4 and TSH. Thiocyanate affects the thyroid by the same mechanism as perchlorate (competitive inhibition of iodide uptake). Steinmaus et al. (2007) analyzed the NHANES data to determine whether smoking status (smoker or nonsmoker), serum thiocyanate, or serum cotinine were better predictors of T4 and TSH changes than perchlorate, or if the effects reflected the combined effects of perchlorate and thiocyanate. These authors found no association between either perchlorate or T4, and smoking, cotinine, or thiocyanate in men or in women with urinary iodine levels >100 μg/l. In addition, Steinmaus et al. (2007) found no association between cotinine and T4 or TSH in women with iodine levels <100 μg/l. However, in women with urinary iodine levels <100 μg/l, they found that an association between urinary perchlorate and decreased serum T4 was stronger in smokers than in non-smokers, and stronger in those with high urinary thiocyanate levels than in those with low urinary thiocyanate levels. The authors concluded that for these low-iodine women, the results suggest that at commonly occurring perchlorate exposure levels, thiocyanate in tobacco smoke and perchlorate

interact in affecting thyroid function, and that agents other than tobacco smoke might cause similar interactions (Steimaus et al., 2007).

Individual Comments

Commenter Name: Carol Bigelow
Commenter Organization: University of Massachusetts
EPA Document ID: EPA-HQ-OW-2008-0692-1427
EPA Comment ID: 20629
EPA Comment Code: 2200

Comment: The analyses that form the basis of docket ID No. EPA-HQ-OW-2008-0692, entitled "Drinking Water: Preliminary Regulatory Determination on Perchlorate" err significantly in the omission of critically relevant data sources. At a minimum, a critical evaluation of Blount et al (2006a) should be incorporated into the docket and the conclusions drawn therein should be revised accordingly.

Another key data source that was omitted from consideration by the EPA is the relationship between perchlorate exposure and thyroid function identified by Blount et al. (Blount et al., 2006a). Blount et al., (2006a) results are consistent with a causal relationship between perchlorate exposure and thyroid function as follows:

a. The strength of the relationship between urinary perchlorate and serum total T4 and serum TSH was greater in women with low urinary iodide (>100 ug/L).

b. The strength of the relationship between urinary perchlorate and serum total T4 and serum TSH was greater in women who smoked (Steinmaus et al., 2007).

c. Significant relationships with other ions known to affect iodide uptake were not observed.

d. Given the known variability in urinary perchlorate levels (Blount et al., 2006b) and in T4 and TSH levels (Andersen et al., 2002; Andersen et al., 2003), a very large sample size would be required to identify these relationships.

EPA cites the NAS report of 2005 (NRC, 2005) as indicating that epidemiological studies cannot identify a causal relationship between perchlorate exposure and thyroid function. However, the CDC study of 2006 represents a verification that known and predicted relationships between perchlorate exposure and thyroid function are occurring at environmental levels of perchlorate exposure in the human population. EPA must consider the statistical power of the CDC study to identify relationships of interest. These findings, furthermore, indicate that the high-dose, shortterm studies of Greer and others do not provide relevant information about the life-time low-dose exposure to perchlorate. Therefore, in the absence of a rational alternative to epidemiological studies to identify such relationships of interest in humans, EPA must employ the best available science - that of the Blount study.

Response:
See response to comment ID 29078 under comment code 2200.

Commenter Name: Rebecca Downey
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1888
EPA Comment ID: 20772
EPA Comment Code: 2200

Comment: The EPA is choosing to ignore and dismiss several scientific studies, including thise from the CDC, that show that Perchlorate can cause serious thyroid disruption in women, children, developing fetuses and newborns. This is especially concerning in the unborn and newborn, as thyroid disruption effects brain development, that can lead to mental deficiences.

Response: EPA has found that perchlorate may have an adverse effect on human health. EPA intends to develop a proposed NPDWR for perchlorate and will consider the best available, peer reviewed data as when we develop the proposed NPDWR.

Commenter Name: Lenny Siegel
Commenter Organization: Center for Public Environmental Oversight
EPA Document ID: EPA-HQ-OW-2008-0692-2019
EPA Comment ID: 20854
EPA Comment Code: 2200

Comment: More important, though it draws upon the work of the Centers for Disease Control to profile perchlorate exposures in the population, it dismisses one of its key findings: In 2006 Blount et al found that women with low iodide levels (over a third of the female population) experience decreased thyroid functions at low perchlorate exposures characteristic of much of the U.S. population. That effect could seriously impair the development of fetuses carried by such women.

But EPA states that Blount did not establish a causal relationship. That is, other factors-such as exposure to nitrates or thiocyanate, might be influencing thyroid function. It wrote, "It is also not known whether the association between perchlorate and thyroid hormone levels is causal or mediated by some other correlate of both."

That is, EPA recognizes that there is a major threat to public health, but it refuses to take action because there is a chance that the association between perchlorate and decreased thyroid function might be caused by another. unknown chemical compound. Yet EPA promises no action to track down and investigate that mysterious cause. This is unconscionable!

Response: See response to comment ID 29078 under comment code 2200

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20901
EPA Comment Code: 2200

Comment: Even with the errors and bias that the use of the CIIT computer model injects into EPA's assessment, EPA still concludes that up to 2 million people may be consuming drinking water that exceeds the HRL, including tens of thousands of infants and young children. The agency then dismisses these impacts as not significant enough to justify setting a drinking water standard for perchlorate. If EPA had used CDC's real world data in it's assessment instead of the flawed computer model, a much higher number of infants, children, and women of childbearing age would be found to be at risk.

Response: See response to comment ID 28608 under comment code 2200. Also, see response to comment ID 20903 in comment code 2200 and response to comment code 5220.

After further consideration of the peer review and public comments, EPA has concluded that the PBPK modeling analysis, in the context of the perchlorate regulatory determination, is useful in examining which life stages are most susceptible to the effects of perchlorate. However, because of limitations, EPA has decided the model does not directly bear on the current decision regarding the need for a NPDWR for perchlorate.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20903
EPA Comment Code: 2200

Comment: Introduction:

In this assessment, EPA relies primarily on a physiologically-based pharmacokinetic (PBPK) model to estimate risks to different populations from perchlorate contamination of drinking water. This approach is somewhat suspect to begin with because it is based on a computer model, rather than on the wealth of data from human studies on perchlorate. Recent large, well-conducted human studies on perchlorate have revealed that exposure to this thyroid toxin is widespread among the U.S. population and that women with lower iodine levels are a particularly vulnerable group, in addition to breast-fed infants and young children.

Response: Several commenters supported the use of the PBPK model to inform the regulatory determination only if the significant limitations of the current model are addressed. For example, the inability of the model to reflect iodide nutritional status was cited by commenters and three of four peer reviewers as an important limitation (USEPA, 2008d). Also, several commenters stated that the risks to breast-fed infants and young children are not adequately addressed by the model. They challenged that the modeling analysis is based on average weight infants and healthy adults, while the sensitive life stages for perchlorate include premature infants and hypothyroid women.

After further consideration of the peer review and public comments, EPA concludes that the PBPK modeling analysis, in the context of the perchlorate regulatory determination, is useful in examining which life stages are most susceptible to the effects of perchlorate. For example, the model indicates that a fetus may be seven times more sensitive to the effects of perchlorate than a pregnant woman. The model also allows for the estimation of the concentration of perchlorate in breast milk (thus breast-fed infant exposure) at various maternal perchlorate exposure levels. However, because of the stated limitations, EPA has decided the model does not directly bear on the current decision

regarding the need for a NPDWR for perchlorate. EPA is continuing to evaluate whether the model could be used in setting a NPDWR for perchlorate.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20909
EPA Comment Code: 2200

Comment: Background

Recent research from the CDC and the Food and Drug Administration (FDA) provide strong evidence that perchlorate exposure among the U.S. population presents potential health threats that justify strong protective measures by public health agencies. The most compelling findings from recent research from government agencies and academic scientists are summarized below:

* CDC tested 2,820 U.S. residents (ages 6 an older) in a nationally representative sample and found detectable levels of perchlorate in the urine of every person tested (Blount et al. 2006a);

* Urinary perchlorate levels in children ages 6 to 11 were 1.6 times higher than levels in adults (Blount et al. 2006a);

* CDC scientists analyzed both perchlorate and thyroid hormone levels in more that 1,000 U.S. women and found that in the one third of women with lower iodine levels, perchlorate exposure far below EPA RfD of 0.7 ug/kg/day was associated with significant changes in thyroid hormone levels (Blount et al. 2006b);

* Using CDC data, an EWG analysis found that 2 million women of childbearing age may be at risk for abnormal thyroid hormone levels during pregnancy (EWG 2006);

* CDC and academic scientists have tested a combined 118 samples of U.S. breast milk in 4 different studies and have found perchlorate in every sample tested (Dasgupta et al. 2008, Kirk et al. 2005, Kirk et al. 2007, Pearce et al. 2007);

* Breast milk studies suggest that a significant number of breast fed infants may be exposed to perchlorate at levels that exceed the EPA RfD of 0.7 ug/kg/day (Dasgupta et al. 2008, Kirk et al. 2005, Kirk et al. 2007, Pearce et al. 2007);

* FDA scientists found perchlorate in three quarters of nearly 300 commonly consumed foods and beverages; young children are exposed to perchlorate doses that fall between 50 to 56% of EPA's RfD from food alone and could easily exceed EPA's RfD with additional drinking water exposures (Murray et al. 2008);

* A recent study from scientists at the University of Texas found that breast tissue concentrates perchlorate at 3 times the rate of iodine (Dasgupta et al. 2008).

This body of data from a number of respected sources including CDC, FDA, and academic scientists provides compelling evidence that establishes widespread exposure to perchlorate among the U.S. population and toxicity in a vulnerable population (women with lower iodine levels). The findings of widespread food contamination are especially concerning for young children, who eat more food and drink more water per unit of body weight when compared to adults.

EPA's decision not to regulate perchlorate in drinking water in the face of such compelling facts is irresponsible and indefensible given the strength of the evidence for stringent regulation. In fact, EPA reached its decision by using flawed models and methodology; following are some of the most glaring reasons that this assessment is inadequate.

Response: EPA agrees that perchlorate occurs at a frequency and at levels of public concern in public water systems and intends to develop an NPDWR for perchlorate.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20912
EPA Comment Code: 2200

Comment: EPA relies on flawed computer model while downplaying significance of human data: As noted above, EPA relies heavily on a deeply flawed computer model that predicts RAIU inhibition at various levels of perchlorate contamination of drinking water. The dependence on such a computer model would be more understandable were there not comprehensive human data on perchlorate exposure and toxicity. However, in the last two years, government agencies like CDC and FDA, as well as prominent academic scientists, have published studies establishing widespread perchlorate exposure among the U.S. population, with especially high exposures among breast-fed infants and young children, and evidence of toxicity among women with lower iodine levels.

CDC published a ground breaking study in 2006 showing that current perchlorate exposures are associated with significant effects on thyroid hormone levels in women with low urinary iodine levels. EPA deliberately downplays the significance of these findings, noting that CDC findings are contradicted by another study: "Results from studies of the effects of perchlorate exposure on hormone levels have been mixed. One recent study did not identify any effects of perchlorate on blood serum hormones (Amitai et al. 2007), while another study (Blount et al. 2006b) did identify such effects" (EPA 2008).

However, when the Amitai et al. study is reviewed, it is clear that the results of this study do not contradict the results from Blount et al.; in fact, the study authors themselves note, "Based on differences in iodine intake and life stages for the two studies, our findings do not contradict those of Blount et al." (Amitai et al. 2007). Yet, EPA maintains that the results from Amitai et al. provide evidence to doubt CDC results although the two studies are completely different and the CDC study is the only one to have established unique vulnerability to perchlorate among women with lower urinary iodine levels. By raising doubts about the validity of CDC findings, despite no scientific justification, EPA is able to downplay the significance of these findings to justify excluding them in their assessment.

Response: See response to comment ID 20909 under comment code 2200. Also see responses to comment IDs 29078 regarding the Blount et al. study and 20903 regarding PBPK modeling under comment code 2200.

Commenter Name: Caroline Baier-Anderson, PhD
Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20946
EPA Comment Code: 2200

Comment: CDC Studies Reveal Relationships between Perchlorate Exposure and Thyroid Hormones that Make Biological Sense

CDC researchers evaluated the relationship between urinary levels of perchlorate (which was found in every individual tested and at significantly higher levels in children, and serum levels of TSH and total T4 in 2,299 men and women, >=12 years of age, participating in the CDC-sponsored National Health and Nutrition Examination Survey (NHANES) during 2001-2002 (Blount et al. 2006, 2007). This study found that:

* All individuals tested were exposed to perchlorate. * Children had significantly higher levels of perchlorate exposure, * For all women >=12 years of age, multiple regression analysis found urinary perchlorate to be a significant predictor of serum TSH and a significant predictor of serum T4. * For women with urinary iodine < 100 ug/L, multiple regression analysis found perchlorate to be a significant predictor ($p < 0.0001$) of T4 with a coefficient for log perchlorate of -0.8917. * Perchlorate was also a significant predictor ($p = 0.0010$) of log TSH with a coefficient of 0.1230.

Hence, the results of the Blount study more closely reflect our understanding of the biological and toxicological processes pertaining to thyroid homeostasis, both in terms of thyroid hormone variability and the role of iodine. The researchers conclude that "[i]ncreased urinary perchlorate was associated with increased TSH and decreased T4 for women with urinary iodine levels < 100 ug/L, a group possibly more susceptible to competitive inhibition of thyroid iodine uptake by perchlorate. The statistically significant associations of urinary perchlorate with decreased serum T4 and increased serum TSH were consistent with competitive inhibition of iodide uptake."

The Blount study also validates findings of previous CDC study that 36 % of women in the National Health and Nutrition Examination Survey (NHANES), 2001-2002, had low iodine intake (< 100 ug/L urinary iodine) (Caldwell et al. 2005) , which translates to approximately 43 million US women (Pirkle 2007).

Response: See response to comment ID 29078 under comment code 2200.

Commenter Name: Caroline Baier-Anderson, PhD
Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20948
EPA Comment Code: 2200

Comment: EPA Fails to Recognize the Importance of Iodine and Individual Variability

On page 60268 of the Federal Register Notice, EPA suggests that a study by Amitai et al. (2007) provides information that contradicts the findings of the Blount study, stating that measured T4 values were not associated with perchlorate levels, despite the fact that the perchlorate levels were much higher than in the CDC study. Amitai et al. directly address this comparison, asserting that because of differences in the study population between the Amitai and Blount studies, the studies are not contradictory:

"A previous study of pregnant women in the coastal areas of Israel indicates iodine sufficiency (urinary iodine median=143 ug=L, mean=130 ug=L) based on World Health Organization (WHO) criteria. Another important difference between the current work and the Blount et al.'s study is the study population: we examined thyroid function in neonates, while Blount et al. studied adults and adolescents. Based on differences in iodine intake and life stage for the two studies, our findings do not contradict those of Blount et al." (emphasis added) (Amitai et al. page 848).

Another earlier study evaluating high levels of exposure to perchlorate (the Chilean study) also involved a population that was iodine sufficient (Tellez et al. 2005). Taken together these studies indicate they iodine sufficiency is a critical component of resistance to perchlorate effects. With over 1/3 of US women demonstrating insufficient iodine intake, iodine status must be considered as an important characteristic of the exposed population.

EPA's failure to appropriately account for both individual variability and iodine status ignores important biological and toxicological considerations and has contributed to the selection of a reference dose that is not adequately protective of sensitive subpopulations.

We strongly recommend that the CDC data analyzed in the study by Blount et al. 2006 and Blount et al. 2007 be used as the basis for the derivation of a new reference dose. One option would be to estimate perchlorate dose from urinary perchlorate using an equation developed by Mage et al 2004 and applied by Blount et al. 2007. EPA could then estimate benchmark doses of perchlorate associated with benchmark responses for abnormally low T4 serum concentrations and abnormally high serum TSH concentrations in women with low urinary iodine excretion. EPA could use the BMD low (representing the lower limit of a one- sided 95% confidence interval), which more accurately reflects the statistical power inherent in the study design than the NOAEL (or NOEL, or LOEL for that matter), and more efficiently utilizes the dose-response data while being less sensitive to the spacing of doses. An uncertainty factor may be necessary to ensure the protection of the fetus and neonate. There are likely to be other approaches to data analysis that accounts for sensitive subpopulations, including individual variability, iodine status and windows of vulnerability and we encourage EPA to re-evaluate these options.

Response: See response to comment ID 29078 under comment code 2200. EPA accounts for individual variability by incorporation of an intraspecies uncertainty factor in the derivation of the RfD.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting

EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20970
EPA Comment Code: 2200

Comment: This value could be further checked against the NHANES data:

The effective perchlorate equivalent NOEL (NOEL3) as explained before is 7.04 + 5.8 = 12.8 ug/kg-day. This, as explained before, leads to a new RfD of 1.28 ug/kg-day applying the same UF of 10.

The background of the other 2 goitrogens represents 40% of NOEL3 (5.8/12.8= 0.4) (and the perchlorate background 0.3%).

Therefore the RfD for perchlorate alone for the general population would be 1.28x 0.6 = 0.77 ug/kg-day and the HRL would be 27 ppb.

This is very close to the 26.7 ppb assigned above as HRL for perchlorate alone in the perchlorate-nitrate cup if the nitrate HRL would also be subject to an UF of 10 and it is also close to the current EPA DWEL of 24.5 ppb.

In any case it would not have much sense as a public health policy and in particular in terms of thyroid protection to try to arrive at the most accurate DW HRL for perchlorate and leave the nitrate MCL at such levels that this effort would be completely nullified.

Therefore it should be recommended to set a joint HRL of 45 ppb perchlorate equivalent for nitrate and perchlorate combined.

Response: See response to comment ID 29078 under comment code 2200. EPA cannot comment on a value for combined nitrate and perchlorate because that has not been peer reviewed.

Commenter Name:
Commenter Organization: Ag Council et al
EPA Document ID: EPA-HQ-OW-2008-0692-1987
EPA Comment ID: 20978
EPA Comment Code: 2200

Comment: The Blount (2006) Analysis of Perchlorate Data has Several Limitations and EPA Should not Rely on its Conclusions to Make Regulatory Decisions.

The argument has been made that the Blount (2006b) results, which show a slight correlation between perchlorate in urine and changes in thyroid hormone levels in women with sub-optimal iodine levels, should be given considerable weight by EPA in making its regulatory determination for perchlorate. This work has several limitations which necessarily impede its use in drawing conclusions regarding the health effects of perchlorate, particularly for purposes of regulatory decision making. Chief among these is the fact that Blount (2006b) does not establish direct causation, only an association between two independent data sets. A number of intervening factors could cause or contribute to the reported decrease in thyroid hormone levels. Moreover, the Blount

(2006b) results conflict with the overwhelming body of scientific evidence showing no effect on the thyroid at environmentally relevant levels. Dr. Blount himself has acknowledged the limitations of his results. Similar concerns have been raised by independent organizations such as the American Thyroid Association.

The California agricultural industry appreciates US EPA's consideration of our comments on its preliminary regulatory determination for perchlorate. We remain committed to working with US EPA, FDA and individual states to preserve the safety of our products and their contribution to balanced, heallthy diets.

Sincerely,

Ag Council California Citrus Mutual California Cotton Ginners and Growers Association California Farm Bureau Federation California Grain and Feed Association California Grape and Tree Fruit League Grower-Shipper Association of Central California Grower-Shipper Association of Santa Barbara and San Luis Obispo Counties Imperial Valley Vegetable Grower Association Ventura County Agricultural Association Western Growers Western Plant Health Association Western United Dairymen

Cc: Benjamin Grumbles, Assistant Administrator, U.S. EPA Office of Water Nega Beru, Director, U.S. FDA Office of Plant Dairy Foods and Beverages Charles F. Conner, Deputy Secretary, U.S. Department of Agriculture

Response: See response to comment ID 29078 under comment code 2200.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-2082
EPA Comment ID: 21024
EPA Comment Code: 2200

Comment: 7. Next, your letter raises the issue of the NHANES 2001-2002 survey results and the Blount et al. 2006b study.

It is important to note that the results of the NHANES survey reveal that the US population is not exposed to levels of perchlorate that could cause an adverse effect, even when all exposure sources - in food and water - are considered. There has been considerable discussion over the role of the Blount study in the regulatory decision-making process. Those who support its use point to the specific finding that perchlorate levels were a negative predictor of total T4 and a positive predictor of TSH in women with urinary iodide less than 100 μg/L. While the findings of the study are interesting, the specific finding at issue is not able to determine causation and is simply based upon an association between two variables. The study directly conflicts with the large number of studies that have shown no effect at environmental levels. Government agencies and private organizations, including the Agency for Toxic Substances and Disease Registry, the American Thyroid Association and the Toxicology Excellence for Risk Assessment (TERA), have identified several limitations concerns with the Blount study. As a result they recommend that based on its status as solely an

associational study and as well as the numerous limitations, it should not be used in regulatory decision-making.

ATSDR (2008) reviewed the Blount et al. (2006b) study in their assessment. ATSDR did not believe that it merited any special consideration over other studies in the well developed perchlorate literature database. They stated that their decision "...was made after a careful evaluation of the NRC report and of studies that have been published after the NRC (2005) report. The results from newer studies do not change the bottom-line recommendation" (ATSDR, 2008).

The lead author, Dr. Benjamin Blount, has acknowledged several limitations with the study and that its results require validation. At an NAS workshop on risk assessment considerations for thyroid active compounds [FN5: National Research Council Fifth Workshop of the Standing Committee on Risk Analysis Issues and Reviews, Risk Assessment Considerations for Interpretation of Bioassay Data and Human Biomonitoring Data for Thyroid-Active Compounds: Issues of Variability, Critical Reproductive-Developmental Periods, and Cross-Species Comparisons, May 15-16, 2008.], Dr. Blount reviewed the results of this study and identified several limitations with the study:

* due to other missing data, perchlorate could be a surrogate for an unknown variable;

* the study is only a cross-sectional association, recognizing that it does not establish a direct causation between perchlorate levels and thyroid hormone levels;

* although this study looked at total T4, free T4 is a better measure, and

* the study was based upon a weak iodine assessment. [FN6: Ben Blount, Biomonitoring Data on Thyroid-Active Compounds: Database and Issues Regarding Variability and Interpretation, presented at NAS workshop in note 1 above, May 15, 2008.]

8. Please see the attached copy of our comments recently submitted to the EPA docket for a more extensive discussion regarding concerns and limitations of the Blount study and its inappropriate use for regulatory decision-making.

Response: See response to comment ID 29078 under comment code 2200.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21038
EPA Comment Code: 2200

Comment: RE: Docket ID No. EPAHQ- OW-2008-0068 Comments on the US Environmental Protection Agency's Preliminary Regulatory Determination on Perchlorate November 28, 2008

I am submitting these comments unanimously since I am employed in an organisation that may not consider these comments acceptable.

Thank you for the opportunity to comment on the USEPA Office of Water's Preliminary Regulatory Determination on Perchlorate.

Comment subject

EPA refers to the Blount et al., (2006b) study and EPA mentions that in that study other covariates were evaluated besides perchlorate.

Of those covariates only 2 were substances that, just as perchlorate, have a potential effect on TSH and T4 levels i.e. nitrate and thiocyanate.

EPA also mentioned that "The researchers state that perchlorate could be a surrogate for another unrecognized determinant of thyroid function".

We would like to comment on the fact that a multitude of other substances exist in the environment that can affect the level of those thyroid hormones and that most probably perchlorate is the surrogate, the marker for this pool of substances and nothing else.

Summary

More than 2 years after the publication of the Blount et al., (2006b) study there exist still doubts and EPA seems to confirm this, that the very low levels of perchlorate, in contrast to the body of literature, would be the cause of the observed thyroid hormone level change.

The following reasoning should eliminate this doubt.

1. Circumstantial evidence

1.1. The effect level found in the Blount study at 10,000 times or 4 orders of magnitude lower than consistently found hitherto in the body of literature is unlikely.

1.2. If it still would be seen as likely, then consequently the current EPA HRL should be divided by 10,000 from 24.5 ppb to 0.002 ppb and even to 0.0002 ppb if an additional UF (uncertainty factor) on top of the NRC UF of 10 would be applied (as has been suggested by some, justified or not).

1.3. Iodine uptake inhibition precedes any adverse health effect of perchlorate exposure including TH (thyroid hormone; here T4 and/or TSH) level change so perchlorate cannot have an effect on TH when there is no iodine uptake inhibition in the first place. Evidence from the NHANES data on which the Blount study was based shows that overall, most probably iodine inhibition did not exist.

1.4. The relationship of 2 other well known iodine uptake inhibitors with TH.

1.4.1. Their "unexpected" relationships Thiocyanate and nitrate show relationships with TH and iodine in an "unexpected" direction and contrary to the perchlorate relationship with TH and iodine which was in the "expected" direction (and then only for iodine insufficient women; the direction was "unexpected" as well for iodine sufficient women).

If those would be assumed to be causal as well - and they should be if the relationship with perchlorate is assumed as such- then the competitive uptake inhibition mechanism as we know it should be discarded and dietary increase of iodine should always be discouraged. The same should be said also regarding the relationship of perchlorate with TH for iodine sufficient women. We have not heard those proposals.

1.4.2. Their strength level The other 2 goitrogens, thiocyanate and nitrate, with the same mode of action as perchlorate do not show this "expected" relationship even though their equivalent levels are 28 and 56 times higher respectively.

Conclusion of 1.4.: If all other relationships found are considered highly implausible(in the opposite direction of what should be "expected") to be causal, what can be the justification to single out one as causal because it seems to fit the "expectations" and explain away all the other relationships as "unclear" since they do not fit those expectations?

2. The number and probability of possible alternative causes

2.1. Why should those possible alternative causes have been considered with priority? Since it was shown that iodine levels overall were probably not relevant we should not look for something that affects NIS (and therefore potentially but only indirectly TH levels) but something that affects TH levels directly.

It is surprising that EPA does not raise this issue but limits itself to mentioning nitrate and thiocyanate. If the Blount et al. study were about iodine uptake inhibition effect then this would have been justified. But it was not.

It was about the downstream effect, the effect on TH.

2.2. Covariates that have not been taken into consideration in the study and should have been so with priority.

There are many widespread contaminants that are goitrogenic with effects on TH levels via mechanisms unrelated to iodine uptake such as organohalogens and other dioxin-like compounds which are ubiquitous and include many pesticides as well.

They act thru different mechanisms.

Only PCBs already include 209 congeners that vary based on the number and positions of chlorine atoms.

Other substances such as Bisphenol-A , methylmercury are believed to be goitrogenic, even halogens like bromide or fluorine added in drinking water (besides chlorine) or their reaction products. Added to these should be natural goitrogenic substances such as isoflavones, genistein, resveratrol, silymarin and linuron.

Data on some were available in the same 2001-2002 NHANES database from which perchlorate, iodine and the other 2 NIS goitrogens were extracted.

Many studies including several EPA sponsored studies deal with those other goitrogens; some even include perchlorate in parallel.

The question should then be asked: why were those goitrogens not controlled for or at least referred to as possible causes?

2.3. The level found compared with the effect level

The known threshold effect level on THs of organo halogens such as PCBs and other dioxin-like substances and their levels in the NHANES 2001-2002 database have been found to be in the same range and some showed a relationship with THs as well.

This is in stark contrast with the 4 orders of magnitude difference for the corresponding levels of perchlorate in the Blount study.

3. What then could be the link between perchlorate and those known endocrine disruptors?

The most obvious and most widely spread common link is chlorine.

On one hand it has been shown that chlorine based disinfectants such as those found in drinking water (DW) oxidize to perchlorate as a disinfection by-product (DBP).

This is for example the reason why Massachusetts doubled its MCL from 1 to 2 ppb.

This oxidation is significant as it corresponds to about 1/3 of the average daily intake of perchlorate according to the Blount study (from the NHANES data).

Bleach is used ubiquitously as for example in water purification stations, paper mills, drinking water and for many other applications.

Other potential sources of perchlorate as a DBP are other chlorine derivates such as chlorine gas and chloramine.

On the other hand other DBPs originate from the reaction of chlorine based disinfectants with organic matter (waste) to form organochlorides.

There are 2 DBP pathways that link perchlorate and those other goitrogenic substances with chlorine:

DBP road 1: Bleach/Cl2/Cl-/chloramine ->ClO-3 ->ClO-4

DBP road 2: (in presence of organic (C) material):

Bleach/ Cl2/Cl-/ chloramine ->phenols ->organochlorides/dioxins

So chlorine is one example of the link between very low levels of perchlorate and TH affecting substances.

Since organo-chlorinated compounds are ubiquitous and since we find around 1/3 of the total dietary perchlorate where we find organo-chlorinated compounds and since many of those have been shown to affect TH levels it is to be expected that low levels of perchlorate are associated with TH levels as found in the Blount study.

Yet assigning cause to this association would be against all common sense as overwhelming circumstantial evidence points in another direction.

Perchlorate seems to be rather a marker, a witness, a messenger of the presence of ubiquitous goitrogenic contamination caused by the net effect of hundreds of substances (see also next section).

4. Would this be the final answer: organochlorides are the sole cause of the (slight) TH changes? Probably not.

There seems to be a ubiquitous contaminant pool in which there are all kinds of goitrogenic substances acting thru all kind of mechanisms that influence TH levels and thyroid function. Somehow they could be all linked together.

So it seems plausible that perchlorate is a marker of this ubiquitous pool of thyroid function affecting contaminants which means that the more perchlorate is found (outside from the point source contaminations of course) the more goitrogenic the pool will be via the chlorine and halogen link and therefore the more goitrogenic effect on THs will be seen.

5. Conclusion

The answer to the question of what caused the Thyroid hormone changes in the Blount study is: all of the above except perchlorate as seen at those very low levels.

It may be felt as politically rewarding to look for a simple explanation but, from what precedes such a simplistic and irrational interpretation would certainly not lead to effective health protective measures. On the contrary it would lead to a feel good situation with only illusory effects.

A careful analysis should precede any sweeping statements like those we are seeing in some media. We hear a lot about holistic approaches in health risk assessment but not many practical applications. This may be one of them.

Response: See response to comment ID 29078 under comment code 2200.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21039
EPA Comment Code: 2200

Comment: In trying to establish a HRL (Health Reference Level) for drinking water, EPA seems to be torn between the 2005 NRC RfD (reference dose) [see reference 1], referred to as "NRC RfD "

hereafter, and a subsequent study [see reference 2], referred to as "Blount" hereafter, that, on first sight, appears to undermine this very RfD.

This study showed a relationship between extremely low levels of perchlorate and TH (thyroid hormone; here T4 and/or TSH) levels.

As a result this relationship has been considered by many as a cause effect relationship suggesting (adverse) effects at a level of perchlorate much lower than that of the NRC RfD, which itself is based on the body of literature.

All kind of erudite and highly complex reviews came out during the following 2 years either supporting or weakening the perceived consequences of this new finding.

Did all this bring us today one step closer to an explanation of this significant contradiction? No, it did not.

Yet it is abundantly clear that there is an evident overall fallacy that has not been exposed. EPA rightly points out, as many have done before, that a cross- sectional study, such as the Blount study can show associations but cannot decide causes.

The main reason is that it does not allow control for non quantified (measured) covariates or for quantified covariates that were not considered relevant but that should have been.

In order to evaluate the likelihood of this hypothetical cause-effect relationship the following 3 aspects should be appraised:

1. The presence of circumstantial evidence i.e. a collection of facts that, when considered together would conclude in favour or against the hypothesis.

2. The number and probability of possible alternative causes.

3. The link of these alternative causes with the hypothetical cause.

Let's see how those 3 obvious criteria work out.

Response: See response to comment ID 29078 under comment code 2200.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21040
EPA Comment Code: 2200

Comment: 1. Circumstantial evidence

1.1. The 4 orders of magnitude difference in levels From Blount (NHANES 2001-2002) data and regression curves, the average urinary level of 2.84 u, which is found to be related to thyroid

hormone (TH) change, is equivalent to an oral perchlorate dose of approximately 0.00004mg/kg-day.

This is 100 times lower than the dose of 0.004 mg/kg-day that was found to be without effect not even on iodide uptake [see reference 1] and which led to the NRC RfD.

Further this dose of 0.004 mg/kg-day on itself is about 100 times smaller than 0.5mg/kg-day, the dose found to have no effect on TH [see reference 1].

So, in stark contradiction to what was found in the body of the literature, the Blount study would suggest, if the relationship perchlorate /TH would be seen as causal, that perchlorate is 10,000 more potent than formerly found.

[see figure in PDF docket ID EPA-HQ-OW-2008-0692-1990]

The following illustrates the effect of 4 orders of magnitude: A dose of perchlorate used to treat Graves disease (excess thyroid function) and which was known since decennia to be effective at about 700 mg/day or 10 mg/kg-day would all of a sudden be effective at 0.001mg/kg-day, a dose that is not only 10,000 times lower than prescribed but also 500 times lower than the dose that only may start to have the intended effect but on euthyroid people instead (0.5 mg/kg- day). At that time would it have been likely that a 10,000 times overdose would have been recommended during several decades knowing that the side effects finally caused this remedy to be pulled from the market? This is highly improbable to say the least.

Another image for the most tenacious readers: To make it more visually comprehensible for their readers, the NRC RfD of 0.0007 mg/l has often been expressed in the media as "a couple of drops in an Olympic seized swimming pool".

The 10,000 times lower dose would then mean that about 9900 swimming pools of that size should be first build in the U.S. before it would be possible to further dilute those same couple of drops to this level since there are only about 100 of those pools existing..

In any case if this first massive conflict would still not be considered relevant or convincing (for reasons that then should be explained however) and the extremely low level causal effect would still be seen as probable then at least the consequences should be consistent which leads us to the second circumstantial evidence:

Response: EPA cannot comment on the calculations by the commenter that have not been peer reviewed.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21041
EPA Comment Code: 2200

Comment: 1.2. The new MCL that should be recommended accordingly

This means the RfD and the corresponding MCL (or HRL) should be lowered accordingly and not from 24.5 ppb to, say, 1 ppb (half the Massachusetts MCL, the lowest state MCL) but to 0.24 or 0.024 ppt (if applying an UF of 10 or 100 respectively) or 0.0002 / 0.00002 ppb.

We have not heard this claim. If this causal relationship would nevertheless exist then this corresponding low level should be suggested as an MCL or HRL. Yet the lowest MCL we have seen proposed in relation to this "new finding" was only about 10-50 times lower than the NRC RfD. This shows that even the most enthusiastic believers don't really belief in it.

When it is too bad to believe, it probably isn't.

Besides, since perchlorate is, just as nitrate, also naturally found in many drinking water wells in the US, particularly in the west and centre of the country at levels about 1000 to 10,000 times higher(between 0.1 and 1 ppb) than this "new" level, one wonders then what effect should this have on the TH status of the millions of people in those areas if such much lower levels would have an effect already.

Response: See response to comment ID 20772 under comment code 2200.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21042
EPA Comment Code: 2200

Comment: 1.3. A downstream effect implies an upstream effect

Adding even more to this discrepancy was the fact that the NRC RfD was based on an effect upstream from the Blount study effect.

Indeed since iodine uptake inhibition precedes any adverse health effect of perchlorate exposure including TH level change [see reference 1], perchlorate cannot have an effect on TH when there is no iodine uptake inhibition in the first place. This is the essence of the iodine uptake inhibition mechanism leading to a (potential) effect on TH levels.

Unfortunately information about possible Iodine uptake inhibition into the thyroid at such low levels, while highly improbable as shown above, was not available from the NHANES data on which the Blount study was based. - Yet what we do know from those data is that there exists a strong relationship between those low levels of urinary (U) perchlorate and U iodine: for an increase of 1 ug/l U perchlorate, the U iodine levels increase linearly with about 30 ug/l all the way from the first to the ninth decile. So, even if perchlorate would have had a potential effect at such low levels it should have been more than compensated by the iodine association as this is what should be expected from a competitive uptake mechanism and because of the fact that the perchlorate inhibitive potency in relation to iodine is known to be around 1/30 based on in vitro studies [see reference 3] or 1/3 in a recent publication based on a in vivo study [see reference 4].

The scatter plot below [see reference 5] illustrates the strong relationship, all the way to the 9th percentile, of very low U perchlorate with U iodine in the U.S. population (NHANES 2001-2002) controlled for THs.

[see figure in PDF docket ID EPA-HQ-OW-2008-0692-1990]

There may be even an explanation for this: perchlorate and iodine are both naturally present in all soils and low levels of perchlorate [see reference 6] and iodine are continuously formed in the atmosphere (just as the other halogens including iodine [see reference 7] and nitrate by the way). The complete disappearance of the relationship in the 9th percentile could be explained as the appearance of the higher level but less diffuse contaminant point sources of perchlorate on top of this natural background.

- Further the same NHANES data show that U iodine is not related with (serum) TH [see reference 8] which implies that the TH level changes observed seem to be caused by something that does not have anything to do with iodine levels and therefore with iodine uptake inhibition. If the TH levels found are independent from iodine U levels and therefore from the levels present in the diet then the downstream TH changes cannot be caused by an iodine uptake inhibitor such as perchlorate. If that still would be the case then iodine supplements should not be recommended for iodine insufficient individuals; again this does not have any sense.

This association unfortunately was not discussed in the Blount paper as the population was split in 2 groups based on their U iodine levels (this confirms that the mind was set on iodine uptake inhibition and not on any other mechanism, see next section).

Response: See response to comment ID 29078 under comment code 2200 regarding the Blount et al. study. As discussed in the final determination, EPA believes that perchlorate may have an adverse effect on human health.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21043
EPA Comment Code: 2200

Comment: What other circumstantial evidence we have?

What about some other covariates?

1.4. Covariates that have been taken into consideration in the Blount study

1.4.1. Relationships of other goitrogens with THs

To be consistent, if the relationship of perchlorate with TH would be considered causal without any supportive evidence then the relationship of the other goitrogens with the same effect on iodide uptake and TH levels should be considered causal as well.

1.4.1.1. Now in this study it was also found that increased levels of thiocyanate were significantly associated with decreased thyroid activity i.e. an unexpected opposite association compared with perchlorate's association. Would that then mean that if this study were about investigating thiocyanate's effect on TH (i.e. not focused on perchlorate) it would have to be concluded that it was now a remedy instead of a goitrogen and that for example consuming cassava would now be good for fighting goitre? Since the opposite is known, this is further strong circumstantial evidence against the causal association.

1.4.1.2. Also nitrate, also a known goitrogen with effect on iodine uptake and therefore, tested (controlled for) as a covariant as well, was significantly associated with T4 levels but only for women with iodine levels considered as sufficient (=100 ug/l) and not for those with levels considered as insufficient. Isn't that contrary to the known mechanism associated with goitrogens as iodine uptake inhibitors? Or how can it be explained that sufficient becomes now insufficient and insufficient becomes now sufficient?

Again the question can be raised: if this were instead a study on the goitrogenic effects of nitrate wouldn't this association, if causal, preclude iodine supplements as a remedy and therefore also preclude iodine as a remedy against perchlorate and thiocyanate? We have not heard this and that would be unlikely and thus further undermines the causal hypothesis.

1.4.1.3. This would then also be in direct conflict with the recommendations we have seen in relation with this study in that iodine insufficient individuals should increase the dietary intake of iodine to compensate for the alleged perchlorate effects.

1.4.1.4. Moreover the fact that perchlorate was associated with T4 also for U iodine sufficient women all the way to the highest levels (besides for iodine insufficient women) would lead to the same contradiction.

1.4.1.5. Most or all of the above statistically significant relationships could only be plausibly causal if the currently generally accepted knowledge about iodine and NIS (Sodium Iodine Symporter) goitrogens in association with the thyroid would be rejected.

We have not found any author bringing forward this new hypothesis about the mechanism related to NIS either.

This overwhelming direct and indirect evidence that the above relationships with other goitrogens could not be causal implies once again that attributing a cause-effect aspect to the perchlorate TH relationship because it happens to be in the "expected" direction, is arbitrary and unreasonable.

Or said in other words, if all other relationships found are considered highly implausible to be causal, what can be the justification to single out one as causal because it seems to fit the "expectations" and explain away all the other relationships as "unclear" [see reference 2] since they do not fit those expectations?

Response: See response to comment ID 29078 under comment code 2200.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21044
EPA Comment Code: 2200

Comment: 1.4.2. Levels of other goitrogens compared to perchlorate.

1.4.2.1. Thiocyanate compared to perchlorate The average U level of the goitrogen thiocyanate is 1,200 ug/l which, after applying a potency equivalency of 1/15 [see reference 2,3], translates into 80 ug/l perchlorate equivalency or 28 times more than the average perchlorate level of 2.8 ug/l.

If 28 times more perchlorate equivalent does not show an association in the "expected" direction how could it be explained that 28 times less does?

1.4.2.2. Nitrate compared to perchlorate The average U level of the goitrogen nitrate is 38,000 ug/l which, after applying a potency equivalency of 1/2402, 3, translates into 158 ug/l perchlorate equivalency or 56 times more than the average perchlorate level of 2.8 ug/l.

If 56 times more perchlorate equivalent does not show an association in the "expected" direction as there is interaction with iodine levels but in the "wrong" direction, how could it be explained that 56 times less does?

It should be noted that the perchlorate potency compared to iodine has recently shown to be much weaker in vivo than in vitro yet the relative potency of the goitrogens compared to each other has been shown to remain unchanged [see reference 4].

Conclusion: Circumstantial evidence overwhelmingly concludes against the hypothesis.

Response: EPA does not believe that sufficient data exist to permit comparison of the relative potency of perchlorate to other goitrogens, or to permit the conduct of a cumulative risk assessment. See response to comment ID 29078 under comment code 2200.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21045
EPA Comment Code: 2200

Comment: 2. The number and probability of possible alternative causes

2.1. Why should those possible alternative causes have been considered with priority?

Above we have discussed the goitrogens that have the same mode of action as perchlorate i.e. inhibition of iodine uptake thru NIS (sodium iodide symporter).

There exist many other goitrogenic substances (which in effect are also goitrogens as they lead to the same endpoints) that have a different mode of action not related to iodine.

The Blount study is about possible effects on THs of substances present in the population sample. So all known substances that affect TH levels should have been statistically tested and controlled for as well and not only those that act through the same mechanism as perchlorate.

Since as shown iodine levels are probably not relevant we should not look in the first place for something else that affects NIS function (and therefore potentially but only indirectly TH levels) but something that affects TH levels directly.

EPA's current RfD for perchlorate is based on perchlorate's ability to inhibit the thyroid gland's uptake of iodide by competing for the sodium (Na+)/iodide (I-) symporter (NIS), the protein responsible for transporting iodide into the thyroid gland for the purpose of synthesizing thyroid hormones.

So it is surprising that EPA does not raise this issue but limits itself to mentioning nitrate and thiocyanate. If the Blount et al. study were about iodine uptake inhibition effect then this would have been justified. But it was not. It was about the downstream effect, the effect on TH.

Yet in the Blount study it was assumed that iodine uptake inhibition was the upstream effect so much so that, as said, the population had been split into 2 groups, iodine deficient and iodine sufficient. As noted before, this only added more inconsistencies as it exposed additional "unexpected" relationships which should have been seen as an additional warning that something was amiss.

Hence substances that have a direct effect on TH should have been tested with priority instead.

Response: See response to comment ID 21044 under comment code 2200.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21046
EPA Comment Code: 2200

Comment: 2.2. Covariates that have not been taken into consideration in the study and should have been so with priority

We quote from the January 2008 Thyroid journal: "Toxicological models and limited epidemiological studies have indicated that many organohalogen aromatic compounds, including dioxins, polychlorinated biphenyls (PCBs), and polybrominated diphenyl ethers (PBDEs), may be classified as â€˜â€˜endocrine disruptors, as they have the potential to alter normal thyroid function." "Because environmental exposures rarely occur singly, it is often difficult to disentangle a single exposure from other cooccurring environmental exposures and conditions that may confer risks upon children. Therefore, there is often the potential for confounding, in which both the exposure and the outcome under investigation are related to a third factor that may distort the observed exposure-disease relationship." "In epidemiologic studies, it is critically important to identify, measure, and control for such confounders."

As mentioned, there are many widespread contaminants that are goitrogens with effects on TH levels via mechanisms unrelated to iodine uptake.

Some can be expressed as TEQ's (total toxic equivalents) and include the known endocrine disruptors such as PCBs (polychlorinated biphenyls), PCDDs (polychlorinated dibenzo-pdioxins), PCDFs (polychlorinated dibenzofurans) besides PCDFs, PBDEs (polybrominated diphenyl ethers), DDE (dichlorodiphenyldichloroethylene) TCDDs (tetrachlorodibenzo-pdioxin), TBBPAs (Tetrabromobisphenol A), degradation products of DDT such as HCB (Hexachlorobenzene), etc. [see reference 9, 10 ,11]

Most of them have a structure resembling thyroid hormones [see reference 12].

They act thru different mechanisms [see reference 13].

PCBs include 209 congeners that vary based on the number and positions of chlorine atoms. Compared with estrogens and antiandrogens, thyroid-disrupting chemicals are the least well studied endocrine disruptors (ED). It is therefore not surprising that few mixture studies exist using this kind of agents.

Further many other substances with completely different structures are known goitrogens in the sense that they also affect directly or indirectly TH levels (see section 4).

Question: Why weren't these substances tested and controlled for as covariates to evaluate the independence of the perchlorate relationship, the more so that the data on some, such as PCBs and other dioxin-like substances, including those concerning pesticides, were available as they were included in the same 2001-2002 NHANES database from which perchlorate, iodine, the other 2 NIS goitrogens and other 12 tested covariates were extracted?

here were other hints that pointed to a different direction: While NHANES 2001-2002 THs levels do not reflect urinary iodine concentrations [see reference 5], serum PCBs, p,p'-DDE and HCB predict Thyroid Hormone Levels [see reference 14] and some do so in NHANES 2001-2002 as well [see reference 15] Also co variants such as smoking status which were associated with thiocyanate in the Blount study and follow-up studies [see reference 16] could just as well be linked to organohalogens as cause since tobacco contains organohalogen pesticides that are organohalogen based or transformed in such substances during burning [see reference 17].

Also why doesn't EPA itself refer here to those critical covariates as they did in the EPA coauthored document: Moving Upstream: Evaluating Adverse Upstream Endpoints for Improved Risk Assessment and Decision-Making, EHP, 2008 and other EPA studies? [see reference 18, 19, 20].

Also reference [see reference 12] that dealt with perchlorate and PCBs as EDs together was research sponsored by an EPA grant.

Why would for example investigating the effects on TH levels of a certain pesticide in soya without controlling for say isoflavones (see further below) or vice versa not be acceptable and why would it be in the case of perchlorate, particularly at such extremely low levels.

Response: The hypothesis tested for in the Blount study was that there was a relationship between perchlorate and a limited number of other goitrogens, iodide status, and TSH/T4 concentration in the samples evaluated. The additional analyses noted by the commenter are beyond the scope of the Blount study. EPA relies upon the best available peer reviewed data. See response to comment ID 21049 under comment code 2200.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21047
EPA Comment Code: 2200

Comment: 2.3. The level found compared with the effect level

The known threshold effect level on THs of organo halogens such as PCBs and other dioxin like substances that has an effect on THs has been found to be in the range of 0.1 to 10 ug /l serum depending on the substance [see reference 21].

The levels of those substances found in NHANES 2001-2002 is in this range and, as mentioned, a relationship of some with THs was found as well [see reference 15].

This is in stark contrast with the 4 orders of magnitude difference between the effect level of perchlorate on THs known from the body of the literature and the perchlorate levels that were related with THS found in the Blount study.

This is illustrated by some scatter plots [see reference 5]:

Scatterplot 1 and 2: the sum of 24 PCBs [see reference 5] has a similar relation with TSH as does perchlorate and for the same range of concentrations (The PCBs are concentrated at the left because of the detection limit). The 2 relationships are statistically significant.

[see figures in PDF docket ID EPA-HQ-OW-2008-0692-1990]

Response: EPA cannot evaluate calculations presented by the commenter that have not been peer reviewed.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21048
EPA Comment Code: 2200

Comment: 3. What then could be the link between perchlorate and those known endocrine disruptor.

The most obvious and most widely spread common link is chlorine. On one hand it has been shown that chlorine based disinfectants such as those found in drinking water (DW) oxidize to perchlorate as a disinfection by-product (DBP).

This is for example the reason why Massachusetts doubled its MCL from 1 to 2 ppb because otherwise chlorination of DW and swimming pools with for example bleach would have to be curtailed.

Is this oxidation of perchlorate from bleach (hypochlorite and hypochlorous acid) significant in comparison with daily intake of perchlorate?

According to the Blount study (from the NHANES data) the average urinary perchlorate level in the population is 2.84ug/l which is roughly equivalent to an oral dose of 0.04 ug/kg-day. This corresponds with drinking water of 1.4 ppb. Massachusetts' MCL was based on data that showed that about 0, 5 ppb perchlorate originated from bleach alone [see reference 22].

Therefore about 1/3 of the average daily intake of perchlorate would be due to bleach oxidation alone which is substantial and which shows that chlorine could be a significant source of perchlorate.

Bleach is used ubiquitously as for example in water purification stations, paper mills, drinking water and for many other applications.

Other potential sources of perchlorate as a DBP are other chlorine derivates such as chlorine gas and chloramine.

On the other hand other DBPs originate from the reaction of chlorine based disinfectants with organic matter (waste) to form organochlorides [see reference 23].

What could be one of the possible pathways that link perchlorate to organochlorides such as PCBs via chlorine?

According to EPA the building block for organochlorides is chlorophenol and chlorophenols are produced from the organic matter found in used water when it reacts with chlorinated disinfectants [see reference 24] (phenol is benzene with a hydroxyl group and PCBs are basically 2 chlorinated benzene rings).

Those DBPs are found back in the drinking water leaving the water purification plants just as perchlorate when no special perchlorate removing devices are used which is the case most of the time in areas where only low levels are found.

So this is one example of the link between very low levels of perchlorate and TH affecting substances: chlorine based disinfectants such as bleach, Cl2 and chloramines evolve to perchlorate on one side and to phenols, PCBS and other organochlorides including dioxin-like compounds on the other side.

[Chloramines, besides being an added disinfectant, can also be formed as a reaction product of bleach with ammonia, itself amply present in used water [see ref 25]].

Response: EPA discussed the potential for perchlorate to be introduced into drinking water as part of the May 1, 2007 FR Notice. However, the source of perchlorate contamination is not a key factor in the determination under SDWA to regulate a contaminant. The presence of perchlorate in disinfectants will be a factor evaluated by EPA as part of the treatment and technology evaluation for the proposed NPDWR for perchlorate.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21049
EPA Comment Code: 2200

Comment: Summary of chapter 3

DBP road 1: Bleach/Cl2/Cl-/chloramine ->ClO-3 ->ClO-4

DBP road 2: (in presence of organic (C) material):

Bleach/ Cl2/Cl-/ chloramine ->phenols ->organochlorides/dioxins

Since organo- chlorinated compounds are ubiquitous and since we find at least 1/3 of the total dietary perchlorate where we find organo-chlorinated compounds and since many of those have been shown to affect TH levels it is to be expected that low levels of perchlorate are associated with TH levels as found in the Blount et al study.

Yet assigning cause to this association would be against all common sense as overwhelming circumstantial evidence shows in another direction.

Perchlorate seems to be rather a marker, a witness, a messenger of the presence of ubiquitous goitrogenic contamination caused by the net effect of hundreds of substances (see also next section).

This alternative explanation would on the same time eliminate any and all contradictions as listed from section 1.1. to 1.4.2.2 above.

Response: EPA does not believe there are sufficient scientific data currently available to assess and characterize the combined risk of goitrogenic compounds. EPA has committed to a drinking water strategy that outlines four principles to expand public health protection for drinking water (USEPA, 2010b). One of these principles is to address contaminants as groups. However, EPA does not believe that regulatory action to address perchlorate should be further delayed. Therefore, EPA intends to develop a proposed rule for perchlorate. At such time as a NPDWR is promulgated, EPA is required to review and revise, as appropriate, its drinking water standards at least every six years. Any revision must at least maintain or improve public health protection. When there are sufficient scientific data to assess the cumulative risks of perchlorate and other contaminants, EPA will review this information to evaluate whether any revisions of NPDWRs are appropriate.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21050
EPA Comment Code: 2200

Comment: 4. Would this be the final answer: organochlorides are the sole cause of the (slight) TH changes?

Probably not.

The fact that in the NHANES 2001-2002 database organochlorides are cross- sectionally associated with THs and, contrary to perchlorate, at levels that are consistent with known effect levels and, contrary to perchlorate, that this does not occasion related inconsistencies if the relationship would be seen as cause effect, still does not mean it is so.

What we only can say at this point is that the chance that those contaminants are at least partially the cause is much higher than for perchlorate.

There seems to be a ubiquitous contaminant pool in which there are all kinds of goitrogens acting with all kind of mechanisms that influence TH levels and thyroid function.

Somehow they could be all linked together.

Following an example of such a link:

When bromides are used as disinfectant also organobromides are formed [see reference 21].

When bromine and chlorine is involved, halogenated furanones can be produced in drinking water by the reaction of naturally occurring organic matter and bromide with the disinfectant chlorine and chloramine. Research on their concentrations in drinking water is at an early stage and they are not regulated by EPA: http://pubs.acs.org/cen/news/86/i13/8613news7.html

[Clarification: A furanone is a furan where the H is substituted with Cl, becoming polychlorinated furanones or polychlorinated dibenzofuranones. A furan is short for dibenzofuran; a chlorinated dibenzofuran is a PCB with a furan ring in the middle]

So the halogen bromine can join the second pathway for chlorine: Bleach/Cl2/ Cl2/Cl-/ chloramine, bromides ->furanones or phenols ->organohalogens/dioxins

This can be illustrated again thru NHANES data plots:

Scatterplot 3 and 4 [see reference 5]: the organobromide PDE (polybrominated diphenyl ethers) has a similar relation with TSH as does perchlorate and for the same range of concentrations. The 2 relationships are statistically significant. Thus organochlorides, organobromides and perchlorate seems to be related with each other within the goitrogenic pool.

[see figures in PDF docket ID EPA-HQ-OW-2008-0692-1990]

Some components of this goitrogenic contaminant pool have a stimulatory or agonistic effect, others an inhibitory or antagonistic effect [see reference 26, 27]. Some do not have any effect at all at environmental doses.

This may explain why in cross sectional studies as those based on the NHANES data base the effect of the sum of some PCBs apparently is not always greater than each individual effect as would be expected [see reference 28] as each individual PCB on itself can be linked to other non identified and quantified goitrogens i.e. (once again) not controlled for covariates with opposite effects.

As mentioned, already there exist 209 known congeners of PCBs alone. They vary based on the number and positions of chlorine atoms but also on their effect (strength and direction).

Many have not even been studied on their goitrogenic effect.

Even different groups of chemicals with different mechanism could have synergetic or antagonistic effects [see reference 29].

Others may be linked to each other in certain environments and not in others.

Going back to the example above: Polychlorinated Biphenyls (PCBs) and Polybrominated Diphenyl Ethers (PBDEs) (both also called polyhalogenated phenolic compounds) may have a cumulative effect where bromine and chlorine based disinfectants are used (for example for swimming pools) and end up as DBPs (disinfection byproducts) in drinking water after having gone thru the purification plant. This link could not exist in places where one of both is not used.

Other goitrogenic phenols, such as Bisphenol A, linked itself to polyvinylchloride (PVC) such as used in waterpipes, may be linked to this chloride and halogen pool. On the other side completely different types of goitrogens, even natural ones, could be linked indirectly to the pool as well: for example organohalogen based pesticides may be present in very low amounts in soybeans but the goitrogenic effect could instead be primarily due to the isoflavones naturally present in soymilk [see reference 30] or the thiocyanates present in rape or broccoli or other natural goitrogens such as genistein, resveratrol, silymarin, linuron [see reference 24].

Also fluorine is considered a goitrogen [see reference 31]. So, adding fluorine in salt for dental purposes could partially neutralise the effect of added iodine. Adding fluorine, another halogen, in drinking water, which is also common, would then on itself be linked to perchlorate and the organohalogen DBPs.

Further fluorine is a major constituent of phosphate fertilizers [see reference 32] and is taken up by the crop so it could, just as the goitrogenic pesticides and isoflavones, be part of the goitrogenic pool as well. Also iodine itself, the fourth halogen, is used as a disinfectant.

Other factors, even the most unexpected (birth delivery mode) may confound the effects [see reference 33].

So it seems plausible that perchlorate is a marker, but only marker, of this ubiquitous pool of thyroid function affecting contaminants which means that the more perchlorate is found (outside from the

point source contaminations of course) the more goitrogenic the pool will be via the chlorine and halogen link and therefore the more goitrogenic effect on THs will be seen.

The answer to the question of what caused the Thyroid hormone changes in the Blount study is: all of the above except perchlorate as seen at those very low levels.

Response: See response to comment ID 21049 under comment code 2200.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1990
EPA Comment ID: 21051
EPA Comment Code: 2200

Comment: It may be felt as politically rewarding to look for a simple explanation but, from what precedes, such a simplistic and irrational interpretation would certainly not lead to effective health protective measures. On the contrary it would lead to a feel good situation with only illusory effects.

A careful analysis should precede any sweeping statements like those we are seeing in the media. We hear a lot about holistic approaches in health risk assessment but not many practical applications. This may be one of them.

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Response: See response to comment code 2200. SDWA requires EPA to rely upon the best available peer reviewed science in establishing a NPDWR.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21066
EPA Comment Code: 2200

Comment: iv. Blount et al. (2006; cited at Blount et al., 2006b in the EPA Notification)

Using the NHANES 2001-2002 data set and a cross-sectional study design, this study reports measurement of urinary perchlorate, urinary iodide, serum TSH, and serum total T4 levels in men and women over the age of 12. The 2001-2002 NHANES data provide the largest group of subjects to date from which sampling data can be derived. The authors report that perchlorate levels were not associated with total T4 or TSH levels in men, but were a negative predictor of total T4 and a positive predictor of TSH in women with urinary iodine less than 100 ug/L. They report that in women with urinary iodine greater than 100 ug/L, urinary perchlorate was a positive predictor of TSH, but not associated with T4. The significance of evaluating women with urinary iodide less than 100 ug/L is based on the WHO statement that a median urinary iodine concentration for the entire population, based on spot samples of less than 100 ug/L is indicative of overall iodine deficiency for that population (WHO 2004).

This study has drawn a great deal of attention as it appears-to the average audience-to demonstrate an "effect" of perchlorate, albeit at exposures below those which cause any measurable inhibition of iodide uptake. However, there are a number of considerations that should be noted that to better understand the significance of the data reported.

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21068
EPA Comment Code: 2200

Comment: Second, it is important to understand what the methods inherent to scientific research are. For example, knowing what is meant by "statistical significance and "clinical significance." A "statistically significant" difference simply means it is unlikely that there is a difference between two variables (e.g., numbers) that is due to chance. With a well designed experimental study, statistical significance can be extremely important. However, statistical significance is also a function of sample size, variability in the variables measured, etc. Statistical significance does not necessarily mean the difference is large, important, or biologically significant. However, for biological data, we are keenly interested if something is statistically significant is it also clinically significant, that is is there change in the variable or parameter that is large enough to affect a clinical or medical condition (e.g., development of hypothyroidism). Blount et al., 2006 report statistically significant variables, but do not report any variables with clinical significance.

This type of study conducted by Blount and his colleagues cannot determine causation, only association between the variables studied (Wartenberg and Buckler, 2001). If important variables are missing, then spurious conclusions can be made. Thus, without a full set of variables measured, including a consistent urinary iodide measurement, any association should be examined carefully for reliability.

Furthermore, perchlorate did not actually lower (or was even associated with) thyroid hormones outside the normal range of values. Even if it had, the NRC committee does not think that "...transient changes in serum thyroid hormones or TSH concentrations are adverse health effects; they are simply biochemical changes that might precede adverse effects" (NRC, 2005).

The study was considered by ATSDR; however, ATSDR states, "limitations of the study acknowledged by the investigators include those common to cross-sectional analyses, the assumption that urinary perchlorate correlate with levels in the thyroid stroma and tissue, and the measurement of total T4 rather than free T4" (ATSDR, 2008).

Third, any study must have careful consideration for the parameters and variables that are measured or available. The purpose of NHANES is designed to collect information about the health and diet of people in the United States. It is a survey for a broad range of possible diseases related to diet and health. While it obtains parameters for thyroid function, those parameters fall far short of the parameters needed to clearly understand thyroid health. For example, there were only two measures of thyroid function (total T4 and TSH) in the NHANES dataset used in this study; NHANES currently uses spot urine samples for iodide status which are neither the preferred, nor most reliable,

measure of urinary iodide (Barr et al. 2005); there was lack of normalization for the dilution of individual urine samples using urinary creatinine levels; and due to restraints of the NHANES database, the authors were not able to note the incidence of autoimmune thyroiditis, the most common thyroid disorder in the U.S., which causes changes in serum T4, T3, and TSH concentrations due to errant immune mechanisms attacking the thyroid gland (NRC, 2005). A complete assessment produced by Intertox is attached as Appendix A. In the appendix, there is a more thorough discussion regarding the use of spot urine testing, confounders, and use of the available NHANES variables to drawn conclusions.

This study did not present urinary measures normalized to creatinine. The concentration of dissolved substances in urine, such as iodide, may vary between individuals or between samples from the same individual. Normalization with creatinine is not a perfect method, but is commonly used to account for this variability (Furnee et al. 1994).

Response: No response is required for the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21069
EPA Comment Code: 2200

Comment: At a recent symposium on perchlorate held in conjunction with the annual Society of Toxicology (SOT) meeting in Seattle, Lamm et al. (2008) presented their initial reanalysis of the NHANES dataset used by Blount et al. with an adjustment for urinary creatinine. Lamm et al. considered a subset of women from the Blount et al. study who were of childbearing age (15-44 years old; the Blount et al. study group included all women over the age of 12) as well as the interaction of thiocyanate and nitrate, both in urine. They found there was no significant association between perchlorate and total T4, even for women with urinary iodide less than 92 ug/g (Figure 2). They did find a significant association for women with urinary iodide greater than 163.7 ug/L for both perchlorate and thiocyanate.

[Figure 1. Urinary Reanalysis Results of the NHANES Data - See PDF Docket ID EPA-HQ-OW-2008-0692-1855]

Response: No response is required to the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21071
EPA Comment Code: 2200

Comment: The American Thyroid Association (ATA) issued a public health statement cautioning against the paper's use in making decisions on regulating perchlorate. The ATA noted that "serum thyroxine was measured as total thyroxine rather than as free thyroxine, the most frequently used clinical measurement and the physiologically available form of thyroxine. Thyroid autoantibodies, an

important confounder in thyroid physiology, have not yet been measured. These have an especially high prevalence in women and may have contributed to the reported correlations. The presence of potentially confounding pharmaceutical and medical factors, such as estrogen use or autoimmune thyroid disease, was not used as a basis for exclusion from the analysis. Inclusion of laboratory results from multiple laboratories may need to be more carefully considered. The reason that perchlorate, but no other measured goitrogen studied, influenced thyroid function at low urinary levels of iodine is not explained. The development of further laboratory information is necessary before the implications of the findings can be understood. The issues raised are important and additional study to resolve them should be pursued" (ATA, 2006).

Fourth, not only were the thyroid hormone values within normal clinical ranges, but urinary perchlorate levels as a surrogate for dose demonstrate that these perchlorate exposures are well below the threshold for zero inhibition of iodide uptake, a non-adverse effect. Exposures that are below the threshold for iodine uptake inhibition are below the NOEL for perchlorate and are not adverse (NRC, 2005; Greer et al., 2002).

Finally, taken from the premise that science is incremental and knowledge builds collectively over time, concerns raised by scientists related to the Blount et al. study should be considered an opportunity for further study. According to Dr. Benjamin Blount, a new study will be conducted using a new data set, NHANES 2007, and will include obtaining data for eight variables of thyroid function (total T4, free T4, total T3, free T3, thyroid globulin, anti-thyroid peroxidase, anti-thyroid globulin, and TSH).[FN5: Personal Communication between Dr. Richard Pleus and Dr. Benjamin Blount. September 22, 2008.] Furthermore, recognizing that urinary spot iodine or single point iodine measures are not a good indicator of iodine status, a different approach is being considered. We believe more research should be conducted to better understand the results of this study.

Response: No response is needed to the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21072
EPA Comment Code: 2200

Comment: Steinmaus et al. (2007) used the same dataset as Blount et al. to assess the correlation between smoking, thiocyanate and urinary perchlorate, and thyroid hormone levels. Using the same NHANES data set, it is not surprising that many of the same results were noted. Many of the same methodological issues reported for Blount et al. apply to this study. As in Blount et al., they did not find any interaction between perchlorate and smoking and TSH or total T4 in women with urinary iodine levels greater than or equal to 100 ug/L or in men. They did conclude that in women with urinary iodine less than 100 ug/L, perchlorate increased the risk of lower total T4 and greater TSH, just as was reported in the Blount et al. study. This association was stronger when the woman was also a smoker or had high urinary thiocyanate levels.

Both Blount et al. and Steinmaus et al. (2007) show an association between exposures to low, environmentally-relevant levels of perchlorate and non-adverse reductions in thyroid hormones that remain within the normal ranges. However, these studies contradict the wide body of direct studies showing no effect even at low levels. These studies are valuable in that they test a large population;

however, neither study shows that exposure to perchlorate at environmentally relevant doses causes an adverse health effect, even in a sensitive population.

Response: See response to comment ID 29078 under comment code 2200. As discussed in the final perchlorate regulatory determination and elsewhere in the response to comments document, EPA believes that perchlorate may have an adverse effect on the health of persons.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21073
EPA Comment Code: 2200

Comment: v. Blount et al. (2007)

Blount and colleagues used the NHANES urinary perchlorate data to estimate the total daily dose for adults. These data were adjusted for creatinine. The estimated 95th percentile dose was 0.234 ug/kg-day with a confidence interval of 0.202 - 0.268 ug/kg-d. They also reported that perchlorate was measurable in all of the samples they tested and the urinary levels were higher in children compared to adults. The estimated doses reported here were lower than the RfD and below the level of inhibition of iodide uptake. The NRC states that "...inhibition of iodide uptake by the thyroid clearly is not an adverse effect; however if it does not occur, there is not progression to adverse health effects" (NRC, 2005).

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21080
EPA Comment Code: 2200

Comment: APPENDIX A

Review of Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL. 2006.

Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environmental Health Perspectives 114(12):1865-71.

A number of scientific issues related to the experimental design of the NHANES dataset and the Blount et al. (2006) analysis make drawing meaningful conclusions from the data extremely difficult. Many of these issues are discussed below, although this list is not exhaustive.

In their paper, Blount et al. (2006) examined the relationship between urinary levels of perchlorate and serum levels of thyroid stimulating hormone (TSH) and total thyroxine (T4) in men and women, aged 12 and older, participating in the NHANES during 2001-2002. They made the following primary observations:

* Perchlorate was not a significant predictor of total T4 or TSH levels in men.

* For women with spot urinary iodine concentrations < 100 ug/L, perchlorate was a significant negative predictor of total T4 ($p < 0.0001$) and a positive predictor of TSH ($p = 0.001$).

* For women with urinary iodine >= 100 ug/L, perchlorate was a significant positive predictor of TSH ($p = 0.025$), but not total T4 ($p = 0.550$).

To assess the reliability of these conclusions, we reviewed the Blount et al. (2006) paper and the NHANES 2001-2002 dataset (CDC 2006) used by the authors. We reviewed the same variables reported in the paper and several dozen other variables not reported in the paper but reported in the NHANES 2001-2002 dataset.

The data collected by NHANES is a survey and not a true epidemiological or clinical study. In epidemiological and clinical studies, effort is made to design the study to control for all variables except the variables in question. Surveys are not designed in this manner-their purpose is to collect data from a large number of people over a period of time. NHANES is designed to assess the health and nutritional status of adults and children in the United States (U.S.), combining interviews and physical examinations. It is a major program of the National Center for Health Statistics (NCHS), which is part of the Centers for Disease Control and Prevention (CDC) of the U.S. Public Health Service, and has the responsibility for producing vital health statistics for the nation (CDC, 2006).

NHANES 2001-2002 was designed to continue the collection of information about the health and diet of people in the U.S. that was begun with earlier surveys to fulfill specific goals. These include estimating the number and percent of persons in the general U.S. population and designated subgroups with selected diseases and risk factors; monitoring trends in the prevalence, awareness, treatment, and control of select diseases; monitoring trends in risk behaviors and environmental exposures; studying the relationship between diet, nutrition, and health; and exploring emerging public health issues.

Response: No response is needed for the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21081
EPA Comment Code: 2200

Comment: Key components to designing a thyroid study

When conducting a thyroid study, a number of key variables should be considered that are not necessarily included when collecting data for a survey such as NHANES. For instance, thyroid hormone and TSH levels can vary substantially during the day. Free T4 (not total T4, which was measured in NHANES) is the most important thyroid parameter for assessing hypothyroidism. Because hypothyroidism is most commonly caused by one's own immune system, parameters used to assess this effect (including serum antibodies to thyroglobulin and thyroid peroxidase) should also be measured (but were not in the NHANES study). In general, the use of NHANES data to draw

conclusions regarding exposures is controversial because of "...the utility of these data to address an existing public health concern, including investigation of etiology, instead of undertaking a study that includes original data collection" (Wartenberg and Buckler, 2001).

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21082
EPA Comment Code: 2200

Comment: Study variables of concern

We were able to confirm the dataset Blount et al. (2006) used in the paper and generally replicate the statistical results obtained by Blount et al. This allows us to examine the experimental design of the study with more confidence. Based on our review, we observed several key variables that caused us to question the conclusions presented in the Blount et al. paper. These variables are summarized below.[FN10: This evaluation is primarily based on the sample of 1,111 women aged 12 and older (i.e., the "study group"), described by Blount et al., from whom urine samples for perchlorate and serum thyroid hormone/TSH concentrations were measured, and excluding those who had a reported history of thyroid disease, were taking thyroid medications or a small subset of other thyroid- active drugs, or had extreme (high) levels of TSH or extreme (low) levels of T4. It should also be noted that total T4 measurements were performed at two separate laboratories which may have introduced some bias.]

Relying upon the urinary iodide measurements for classification of study subjects into "low" or "high" iodine groups is not scientifically appropriate.

* Urinary iodine concentrations in the study group ranged from 6 to 136,161 ug/L. The geometric mean was 127 ug/L (SE = 5.4) and the 5th and 95th percentiles were 22 and 568 ug/L, respectively. Our findings for this group are consistent with the summary of urinary iodine measurements in NHANES 2001-2002 published by the CDC (Caldwell et al., 2005). If taken at face value as representative of chronic iodine nutrition, the upper limits of these measurements likely exceed safe levels and should be a source of some alarm for the CDC. For example, elevated TSH levels and hypothyroidism have been associated with daily iodine intakes in excess of 750 ug/day by adults (NAS 2001). However, these measurements were taken in spot samples and are thus not necessarily indicative of an individual's iodine status.

* Urinary creatinine concentrations were highly variable from subject to subject (range 9 to 774 ng/mL), indicating significant differences in sample dilution and, likely, urinary output.

* The WHO has stated that a median urinary iodine concentration within a population, based on spot samples of <100 ug/L is indicative of iodine deficiency within the population (WHO, 2004). The median urinary iodine concentration for the study population evaluated by Blount et al. (n =1,111) is 133 ug/L. Thus, assuming that iodine deficiency exists within this population is inappropriate- the WHO criteria are not meant to diagnose iodine deficiency in individuals (Borak, 2005). Conversely, the best way to establish individual urinary excretion of iodine (or any urinary

analyte) is to collect 24-hour samples (Bourdoux, 1998). However, without a reliable measure or indicator or iodine status, comparison s make suing this measure could be spurious.

* Figure 1A illustrates the variability in urinary iodine concentrations in the Blount et al. dataset.

[Figure 1A: Variability of Urinary Iodine from Blount et al. (2006) - See PDF Docket ID EPA-HQ-OW-2008-0692-1855]

Response: See response to comment ID 29078 under comment code 2200. EPA does not have sufficient information to evaluate the WHO criteria for iodide status.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21083
EPA Comment Code: 2200

Comment: 1. Characteristics of individual members of the study group vary widely. Because many of these variables could impact overall subject health and, potentially, thyroid hormone or TSH levels, it is impossible to establish causality based on this dataset. The following is a sample of some of these variables-many others, both reported in and not reported in the dataset, could potentially impact thyroid measurements.

* NHANES is a survey designed to assess the health and nutritional status of adults and children in the U.S. It is not a controlled epidemiological study. Up to 3,400+ different variables are reported in the online NHANES 2001-2002 dataset in association with specific study subjects. The potential for spurious associations between variables is significant.

* 48% of those who responded were active smokers (42% reported smoking "everyday" and 6% "some days"; only 301 subjects out of 1,111 study subjects had a reported response to this question). 21% of smokers reported smoking 15 or more cigarettes per day. Smoking status of study subjects under 18 years of age (29% of all study subjects) was not reported due to privacy concerns. In addition, 21% of study subjects reported living in a home with a smoker. Smoking is a known source of thiocyanate and other goitrogens. In smokers, cyanide from cigarette smoking is likely the most important source of SCN- in the body (Tonacchera et al., 2004). Ingbar (2000) states that thiocyanate as well as the pyridine components of cigarette smoke are likely a cause of lower T4 and T3 levels in serum of heavy smokers. Smoking and thiocyanate were found to be significant in a later analysis of the same data (Steinmaus et al., 2007).

* 105 reported being pregnant at the time of the examination. Pregnancy is known to have an effect on thyroid economy with significant changes in iodine metabolism and serum thyroid binding proteins (Lazarus, 2005a; 2005b).

* Although Blount et al. excluded subjects who were taking thyroid medications (e.g., levothyroxine) or certain other thyroid active agents (e.g., propylthiouracil or methimazole), subjects taking any other kind of drug were included. 43% of study subjects reported taking at least one prescription drug within the month preceding their examination interview. This includes subjects taking

medications known to directly affect the thyroid including lithium, amiodarone, and carbamazepine. Many drugs affect tests of thyroid function through alterations in the synthesis, transport, and metabolism of thyroid hormones, as well as via influences on thyrotrophin (TSH) synthesis and secretion. Despite effects on circulating thyroid hormone and TSH levels, few drugs result in important changes in clinical thyroid state, but difficulty in interpretation of thyroid function tests often results. Commonly prescribed drugs including anticonvulsants, non-steroidal anti-inflammatory drugs, steroid hormones and heparin may result in abnormal thyroid function tests in the absence of clinical features of thyroid dysfunction. In contrast, lithium and iodine containing drugs, including radiographic contrast agents and amiodarone, may result rarely in overt thyroid disease (Davies and Franklyn 1991; Gittoes and Franklyn 1995; Wenzel 1996; Daminet and Ferguson 2003).

* Many reported having one of a number of specific potentially severe medical conditions; however, only a limited list of conditions was reported. For example, 14 reported having had heart failure, 3 had a current liver condition, 71 had current or past cancer, 13 had been told at some time they have weak or failing kidneys, and an unreported number (due to privacy concerns, presumably) had hepatitis C. Kidney failure is known to causes alterations in thyroid hormone metabolism known as nonthyroidal illness syndrome (Rosolowska-Huszcz et al., 2005). Hepatitis C patients on interferon therapy were found to be more susceptible to autoimmune thyroid diseases (Muratori et al., 2005).

* 4% of adult study subjects are underweight (per CDC guidelines, BMI <18.5), 20% are obese (BMI >=30 and <40), and 4% are morbidly obese (BMI >= 40). Associations between body weight and thyroid hormone and TSH levels have been reported in obese and morbidly obese individuals (Sari et al., 2003; Michalaki et al., 2006).

* Many report other types of exposures. 16% of study subjects reported using pesticides within their home during the previous month. A small number of women (16) reported using cocaine or other street drugs within the previous year, with one reporting using a drug on a total of 200 days during the previous year- because of the nature of this information, it could be assumed that this statistic is 28 underreported. Illicit drug use status for subjects under age 18 was not reported. Associations between pesticide exposure and changes in thyroid hormone/TSH levels have been reported in some animal studies (Beard and Rawlings 1999; Jeong et al., 2006). T4 levels have been shown to decrease in rats following amphetamine administration (Budziszewska et al., 1996).

* 66% of study subjects reported regularly (five or more times per month) consuming dark leafy green vegetables. Among these, consumption amount varied widely (up to 91 times per month). 48% reported consuming cooked dried beans or peas five or more times per month. Dark green vegetables from the Brassica family (e.g., broccoli, kale) are known to contain high concentrations of both thiocyanate and nitrate, two agents known to cause iodide uptake inhibition (IUI) by the thyroid in the same way as perchlorate. Legumes are also known to contain high concentrations of nitrates.

* 46% of study subjects reported taking dietary supplements during the month preceding their examination interview. 2% (22 subjects) admitted taking a dietary supplement during the fasting period. There is evidence that dietary supplements can affect thyroid function. For example, short-term dietary supplementation with kelp (high in iodine) significantly increases both basal and poststimulation TSH (Clark et al., 2003).

* NHANES 2001-2002 does not report on consumption of soy or soy products. Soy consumption has been associated with development of goiter and an increase in TSH levels in humans (Doerge and Sheehan, 2002). Soy products are heavily marketed to women as healthful, including such products as soy milk, tofu, energy bars and drinks, and meat substitutes. Soy isoflavones (e.g., genistein and daidzein) can also be measured in biological samples such as serum, to give an approximation of soy intake levels.

* Several other important study variables, including location and time of year when samples were collected, were not reported due to privacy concerns. Seasonally-related changes in thyroid hormone concentrations have been shown in adults, with higher T3 and T4 values seen in winter months, and a tendency to a greater TSH response to TSH-releasing hormone (TRH) was noted at this time (Harrop et al., 1985). These changes could reflect a centrally-mediated response of the hypothalamic-pituitary-thyroid axis to environmental temperature (Harrop et al. 1985). Significant annual, four-monthly and biannual rhythms were detected in serum TSH in adults, with the lowest detected in spring. A significant annual rhythm was detected in T3, with lower values in spring and summer than in the other seasons. The peak-trough differences in the yearly variation expressed as a percentage of the mean were 29.1% and 8.2% for TSH and T3, respectively (Maes et al., 1997).

Response: No response is needed for information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21084
EPA Comment Code: 2200

Comment: 2. The "spot" urine and serum samples cannot be relied upon to establish chronic exposure levels or conditions. Spot samples are known to be inherently variable due to variations in urine volume and intake of exogenous compounds, and, in this population, fasting times varied widely between individuals and a substantial percentage of participants did not comply with study fasting requirements.

* For chemicals with a short biological half-life (e.g., perchlorate, iodine), concentrations in spot urine samples are known to be highly variable between samples, due to within- and between-day variations in urine volume and intake of exogenous compounds (Barr et al., 2005). Factors shown to influence concentrations include fasting time, time of day, nature of the last meal, sample dilution, collection method, preservation method, sample interferences, and analytical method (Rasmussen et al., 1999). Urinary iodine concentrations in 24-hour samples vary up to three fold from one day to another. This suggests that a single sample is insufficient to determine long-term iodine status (Rasmussen et al., 1999). Population iodine excretion estimates require 100 to 500 spot urine samples for each group or subgroup and fewer than 10 urine samples in an individual may be misleading (Anderson et al., 2008).

* Serum and urine samples were collected at either "morning" (46%), "afternoon" (36%), or "evening" (18%) examination sessions. Specific sample time of day is not given. In humans, serum TSH concentrations are at their maximum at night, shortly before sleep, about 50-100% greater than the morning low (Fisher, 1996). Early morning values are greater than later morning values (Surks et al., 2005). TSH is secreted in pulses, with eight to fourteen pulses occurring in 24 hours. Sleep

deprivation, strenuous exercise, or working during night or evening shifts accentuate the rhythms (Surks et al., 2005).

* Fasting times were highly variable. Subjects appointed to a morning session were asked to fast for 9 hours while subjects appointed to an afternoon or evening session or a home exam session were asked to fast for 6 hours. However, the protocol states the "greater goal [is] completing as many components as possible within the time constraints of the session with phlebotomy as the highest priority component." Reported length of fast ranged from 0 to 63 hours, with a mean and 50th percentile of 10.3 hours and 5th and 95th percentiles of 1.7 hours and 19 hours, respectively. For the morning, afternoon, and evening sessions, 8%, 13% and 24%, respectively, did not meet the fasting requirement.

* About 2% (22/1111) admitted taking a dietary supplement during the pre-blood and urine collection fasting period. There is evidence that dietary supplements can affect thyroid function. For example, short-term dietary supplementation with kelp (high in iodine) significantly increases both basal and poststimulation TSH (Clark et al., 2003).

* Study participants were allowed to consume diet soda, black coffee or tea with saccharine or Equal since "these have no affect on study analytes." (Protocol p. 4-32). It is relatively clear that sugar substitutes such as those used in diet sodas do not have a significant impact on thyroid function. However, the evidence for a lack of effect with caffeine is less clear. Studies in rats have shown that injection of caffeine results in a decrease in serum TSH followed by a subsequent decrease in serum T3 and T4 (Spindel et al., 1980). However, no effect on thyroid parameters were found in men (TSH and T3) or Syrian hamsters (TSH, T4, and T3) (Spindel et al., 1984; Bartsch et al., 1996).

* Figure 2A illustrates the variability in the fasting times. Though no direct correlation between urinary iodine (and perchlorate) measures and fasting times is seen, it is unclear whether fasting time, exclusive of all of the other variables 30 inherent in this dataset, could have affected urinary concentrations in a well-controlled dataset.

[Figure 2A: Variability of Fasting Times from NHANES 2001-2002 - See PDF Docket ID EPA-HQ-OW-2008-0692-1855]

Response: No response is needed for the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21085
EPA Comment Code: 2200

Comment: 3. The observed differences in perchlorate are that thyroid response between men and women are not explained, which could be due to another unexplained variable. Comparable differences have not been observed in previous studies of perchlorate exposure (e.g., Greer et al., 2002; Braverman et al., 2006; Crump et al., 2000). Missing database variables make it difficult to exclude other possible causes of the observed differences between men and women.

* Thyroid autoantibodies are not measured in NHANES 2001-2002. Women are known to be about 2.7 times more likely to acquire an autoimmune disease than men (Jacobson et al., 1997), and to have a greater incidence of thyroid autoimmunity (Chiovato et al., 1993). Thyroid autoantibody levels have been shown to be positively correlated with TSH levels in humans (Hollowell et al., 2002; O'Leary et al., 2006; Hoogendoorn et al.,2006). In analysis of data from NHANES III, a significant association between female gender and elevated serum TSH levels disappeared when controlled for TPOAb (Hollowell et al., 2002).

* The NHANES dataset does not include a variable directly characterizing time since last pregnancy; this value can be approximated based on reported "age at last live birth" and current age. Using this, about 7.5% of women not currently pregnant reported being pregnant within the previous 2 years. The possibility that postpartum thyroiditis afflicted some of these women cannot be excluded. Postpartum thyroiditis, a syndrome of transient or permanent thyroid dysfunction caused by autoimmune inflammation of the thyroid, occurs frequently in the first year after delivery, with a prevalence of about 5-7% (Muller et al., 2001). In about 25-30% of these women, the condition progresses to permanent hypothyroidism (Lazarus, 2005b).

* Figures 3A and 4A depict the variability in the NHANES data set and the nominal changes noted in thyroid hormones.

[Figure 3A: Variability of Perchlorate in NHANES Data Set - See PDF Docket ID EPA-HQ-OW-2008-0692-1855]

[Figure 4A: Variability of Perchlorate and Changes in Thyroid Horomones - See PDF Docket ID EPA-HQ-OW-2008-0692-1855]

Response: No response is needed for the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21086
EPA Comment Code: 2200

Comment: 4. Spot urine concentrations of nitrate and thiocyanate, two other inhibitors of iodide uptake into the thyroid, were highly variable among study subjects. Since perchlorate, nitrate, and thiocyanate all act through the same mechanism of action (iodide uptake inhibition (IUI) at the thyroid), evaluation of correlations between exposure to iodide uptake inhibitors and thyroid hormone or TSH concentrations should take into account combined exposures to all three anions.

* Perchlorate equivalent concentrations of nitrate, thiocyanate, and perchlorate in urine in the study population (calculated assuming that nitrate is 1/240 as potent and thiocyanate is 1/15 as potent as perchlorate; Tonacchera et al., 2004) ranged from 3.7 to 3329 ug/L. On average, for any given subject, perchlorate comprised about 1% of the total perchlorate equivalent concentration (geometric means are 2.8 and 270 ug/L for perchlorate and perchlorate equivalent concentration, respectively). One would expect to see thyroid effects of nitrate or thiocyanate before seeing perchlorate effects; however, Blount et al. (2006) report no reliable associations between urine levels of nitrate and thiocyanate and serum total T4 or TSH.

* No correlation between perchlorate equivalent concentration and serum total T4 or serum TSH is apparent. Perchlorate equivalent concentration was not a significant predictor of total T4 (p=0.43, coefficient -0.00011) or TSH (p=0.25, coefficient -0.00023). Conceivably, the same problems inherent in relying upon spot urine samples as indicators of longer term iodine intake would affect the reliability of spot urine samples for perchlorate, nitrate, and thiocyanate.

Response: No response required for the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21087
EPA Comment Code: 2200

Comment: Missing Data

Some of the key data related to this study were not accessible in the time frame of this project. For instance, the analytical quality assurance/quality control data is available for review through the National Center for Health Statistics (NCHS), but NCHS requires reviewers to request an appointment and travel to their location to review the data. Other data would need to be obtained under the Freedom of Information Act (FOIA). Key data that could be obtained through these mechanisms might include exact times of blood samples and urine samples, the sequence of sample collection, QA/QC of the analyses, analytical logbooks, and other notes from the survey. These are critical pieces of information that could be useful to characterize the dataset and examine the significance of associations.

Response: No response is needed for the information provided by the commenter.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21088
EPA Comment Code: 2200

Comment: Summary

If one considered this as a pilot study which would be consistent with the stated intended use, then the appropriate and logical next step would be to address a number of these concerns with an enhanced experimental design. For example, adding critical thyroid function variables (e.g., free T4, anti-TPO), 24-hour urine collections, and better control of medications will provide a more appropriate study design.

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Steve Lamm
Commenter Organization: Consultants in Epidemiology and Occupational Health, LLC (CEOH)
EPA Document ID: EPA-HQ-OW-2009-0297-0654

EPA Comment ID: 28486
EPA Comment Code: 2200

Comment: Attached are our comments on perchlorate (10-08-09). The cited references will be submitted separately.

October 8, 2009

Eric Burneson Office of Ground Water and Drinking Water Standards and Risk Management Division Environmental Protection Agency

Re: Docket ID No. EPA-HQ-OW-2009-0297

Comments on Scientific Literature on Public Health levels of concern of perchlorate in drinking water

EPA is considering whether to specifically regulate the level of perchlorate in drinking water and needs to consider the potential adverse effect on human health, the frequency and level of exposure, and whether regulation of the contaminant represents a meaningful opportunity for reducing public health risks. EPA states that it is particularly concerned about the fetus of the iodine-deficient pregnant mother, infants, and developing children."

I review below the literature on the question as to whether the Blount et al. (2006) analysis demonstrates a risk from background perchlorate exposures on "the fetus of the iodine-deficient pregnant mother, infants, and developing children?" I conclude that it does not.

Lamm et al. (2007, under review) demonstrate that the primary Blount finding on perchlorate effect on thyroxine level at low iodine level is dependent on the definition of low iodine as low urinary iodine (<100UG/l) on a single sample. It is not found when creatinine-adjusted urinary iodine level is used as the metric for defining low iodine. Thus, the primary finding is dependent on analytic method and not robust to reasonable variants of definition.

Pearce et al.(2007, 2008 under review) demonstrate that maternal thyroid function is not adversely affected by background levels of perchlorate among first trimester pregnant women from mild or moderate iodine deficient populations or with low urine iodine levels (< 100 ug/L).

Review of published literature is consistent with findings of studies pending publication. Replication of the Blount et al. (2006) type analysis will be possible with the NHANES 2007-2008 dataset.

Regulatory assessment should not be considered independent of these findings. My presentations below provide the bases for the above statements.

Two major issues that I do not deal with here but that must be recognized is (1) that the biological effect proposed by the Blount et al. (2006) analysis is at an exposure level one to two orders of magnitude below that at which effects of perchlorate exposure have been observed and (2) that the issue of iodine adequacy for pregnant women and their offspring in the United states is important, complex, and appropriate for discussion elsewhere.

Is there a negative association between perchlorate and thyroxine with low iodine status?

Blount et al. (2006) is the only report that suggests that there is a biological effect from perchlorate at general US population exposure levels. They have analyzed data from NHANES 2001-2002 and report that women with low urine iodine levels have reduced total thyroxine (tT4) levels associated with increasing levels of urinary perchlorate, i.e., a negative association between urine perchlorate level and serum total thyroxine level among women with urinary iodine level < 100 ug/L. Steinmaus et al. (2007) further indicates that this finding is confounded by smoking.

The Blount et al. (2006) analysis has been interpreted as indicating that the children of women with low iodine status may be at increased risk of neurodevelopment deficit associated with their perchlorate exposure. This is an over-interpretation.

(1) There is no accepted measure for iodine status of an individual within a population. The reference point of 100 ug/L (or 100 ug/g creatinine) refers a population, not an individual. A low urine iodine level in a single urine sample does not equate to a finding of low iodine status.

The usual measure of iodine status is 24-h urinary iodine excretion, and the NHANES datasets do not give that metric. Historically, the 24-h urinary iodine excretion for an individual has been estimated from the urine iodine to urine creatinine ratio (e.g., Rasmussen 1999). This metric could be calculated from the NHANES dataset but is not included in the Blount et al. (2006) analysis. Even that would be a point estimate and not represent the general iodine status of the individual but only the iodine throughput status of that day. Andersen et al. (2001) have shown that single low measurements of iodine level on one day do not demonstrate as an average a low iodine level over multiple specimens over a long period of time (one year).

Laurberg et al. (2007) should get particular attention as it deals with many of the issues confronting EPA on perchlorate and has been developed independent of any perchlorate issues. They succinctly summarize the Andersen et al. (2001) paper as demonstrating that "in a group of people, the distribution of average iodine concentrations in several samples from the same subjects is much narrower than the distribution of values from single spot samples from the same people." They observe that "Only the median or average can be used to classify iodine intake." They conclude that "the concentration of iodine in a spot or casual urine sample cannot be used to diagnose iodine deficiency in an individual."

(2) The Blount et al. (2006) analysis has not analyzed separately these relationships for women of child-bearing age (WCBA, ages 15-44), which would be the relevant population with respect to protecting fetal health.

An analysis of the NHANES 2001-2002 data set for women of child-bearing age using iodine/creatinine as the metric of iodine exposure has examine the relationship of total thyroxine (tT4) with regarding to an association with urinary levels of perchlorate (and the other two iodine-uptake inhibitors, thiocyanate and nitrate) for those with low, medium, and high iodine/creatinine (Lamm et al., 2007). Lamm et al. (2007) has been published in abstract form and is currently under review for peerreview publication.

Lamm et al. (2007) demonstrated that "the negative association of serum thyroxine and urinary perchlorate found for WCBA with low iodine defined by UI (ug I/L urine) was not found for those

with low iodine defined by UICr (ug I/g creatinine)." Their analyses, in contrast, found such an association for WCBA with high iodine/creatinine.

This is not the place to discuss which of these two analyses are "right", but rather to observe that the Blount finding was highly dependent upon the specific metric used to classify low iodine. The lack of robustness with respect to the definition of low iodine suggests that the analytic results are method dependent, rather than a reflection of underlying biology. In this case, it is premature to serve as a basis for regulatory decision-making.

It should be noted that the Lamm et al. (2007 and 2010 pending) analysis of the NHANES 2001-2002 data set demonstrated that a negative association between serum thyroxine level and urinary thiocyanate level was found in WCBA with high iodine level rather than low iodine level, a finding consistent with a similar analysis of the NHANES III dataset (Vanderver et al., 2007). The replication of this finding in a second NHANES dataset is noteworthy. The Vanderver et al (2007) study further uses as its endpoint metric not the serum thyroxine level but the prevalence of hypothyroxinemia, which may be a better metric of outcome.

While the NHANES III dataset did not contain measurements of perchlorate, the NHANES 2007-2008 dataset that is currently being released does. The NHANES 2007-2008 dataset will be appropriate for examining these analytic issues. Analyses of the NHANES 2001-2002 dataset does not resolve them.

Response: See response to comment ID 29078 under comment code 2200.

Commenter Name: Jonathan Borak
Commenter Organization: Yale School of Medicine
EPA Document ID: EPA-HQ-OW-2009-0297-0209
EPA Comment ID: 28507
EPA Comment Code: 2200

Comment: 2). A related, but different issue involves the use of spot urine testing to diagnose individuals as "low iodine intake" or "iodine deficient". I raise this concern for three reasons:

1). The Blount et al. and Steinmaus et al. analyses found significant effects principally in women with spot urine iodine levels <100 ug/L, not in those with spot iodine levels >=100 pg/L. However that 100 ug/L cut-off level is derived from a WHO/UNICEF/ICIDD criterion for determining iodine sufficiency in populations, not individuals.

2). There is a general consensus that "impacts of perchlorate exposure will vary depending upon an individual's iodine sufficiency" (15). Thus, predicting the adverse effects of perchlorate exposure requires knowledge of individuals' iodine sufficiency.

Response: EPA regulatory values and risk assessments are developed to protect the public health at a population level, acknowledging variability in the population as a source of uncertainty. Developing a health protective drinking water health advisory level that protects for potential adverse effects of sensitive subpopulations is EPA's approach to achieving this goal.

Commenter Name: Andria Ventura
Commenter Organization: Clean Water Action et al.
EPA Document ID: EPA-HQ-OW-2009-0297-0528
EPA Comment ID: 28515
EPA Comment Code: 2200

Comment: Moreover, a 1 ppb or lower MCL is supported by the most recent comprehensive studies, and these should be central to EPA's analysis. The industry-supported Greer study, which serves as the basis for EPA's current reference dose as well as California's current 6 ppb standard, consisted of a 14-day study of 37 healthy adults. In more recent years, Blount et al analyzed a nationally representative sample of 2299 U.S. residents, and they have documented anti- thyroid effects in a large population of women exposed to perchlorate at concentrations far lower than levels previously shown to have such effects. This study and subsequent data clearly justify promulgation of an even more protective MCL. It should be noted that California's Office of Environmental Health Hazard Assessment is in the process of reevaluating its Public Health Goal, on which the state MCL is based.

Response: EPA intends to determine the value for the MCLG in developing a proposed NPDWR with consideration of the best available, peer reviewed science. A value for the MCLG has not yet been determined.

Commenter Name: Richard T. Kloos
Commenter Organization: American Thyroid Association (ATA)
EPA Document ID: EPA-HQ-OW-2009-0297-0635
EPA Comment ID: 28531
EPA Comment Code: 2200

Comment: Of great concern to us is the fact that women with low iodine status appear to be at particular risk of perchlorate effects. The study of Blount et al. demonstrated that among the 36% of women with urinary iodine values <100 ug/L in the NHANES 2001-2002 data set, there was a significant positive correlation between urinary perchlorate concentrations and serum TSH ($p=0.001$) and an inverse correlation between urinary perchlorate concentrations and serum T4 values ($p<0.0001$).12 Among women with urinary iodine values >100 μg/L, there was a positive association between urinary perchlorate concentrations and serum TSH ($p=0.025$), but there was no association between urinary perchlorate concentrations and serum T4 values. There were no significant associations between urinary perchlorate concentrations and thyroid function values in men irrespective of iodine intake. Therefore, if the results of this study are correct, the population at highest risk for adverse effects of environmental perchlorate exposure is women with low dietary iodine intake.

Response: EPA agrees that promoting iodide nutrition is good public health policy and may have a positive influence in reducing the iodide uptake inhibition effects associated with exposure to perchlorate. However, the Agency does not think it is appropriate to rely on the promotion of iodide nutrition in this case, especially since these activities are outside of EPA's SDWA authority. While the health concerns associated with perchlorate may be addressed through other means, it is the Administrator's judgment that a standard limiting perchlorate in drinking water can reduce health risk, particularly to fetuses, infants and children.

Commenter Name: John P Gibbs
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0636
EPA Comment ID: 28553
EPA Comment Code: 2200

Comment: 4) THE USE OF THE NHANES DATA AS A POINT OF DEPARTURE

The NHANES 2001-2002 epidemiological urinary data are from a single un-timed spot urinalysis and can vary due to dilution or concentration of the urine (i.e., due to an individual's hydration status). A common technique to eliminate this variation in the spot urinalysis is to normalize the iodide urine concentration against creatinine resulting in the analysis expressing iodide excretion as ug of iodide/g of creatinine (i.e., ug/g creatinine) instead of ug of iodide/L of urine. Lamm has successfully repeated Blount's statistical analysis of the NHANES 2001-2002 epidemiological data only when his analysis measures UIC as ug/L (Lamm 2007). However, when Lamm 2007 repeats the statistical analysis using only women of childbearing age (ages 15-44 years) and UIC measured as ug/g creatinine, the statistical significance of the relationship between decreasing tT4 with increasing perchlorate exposure in women with low UIC is lost. The statistical significance of this relationship should be present regardless if the analysis expresses UIC in ug/L or ug/g of creatinine. This inconsistency suggests that the relationship between tT4 and perchlorate reported in the Blount analysis might be an artifact in the NHANES data set. The figures below show significant scatter in the perchlorate vs T4 and TSH correlations from the NHANES datset and cast considerable doubt on the clinical significance of any statistical significant findings reported by Blount et al 2006.

[Figure. Gender groups - Perchlorate vs T4 - see PDF docket ID EPA-HQ- OW-2009-0297-0636]

Additionally, studies among pregnant women do not demonstrate a correlation between urine perchlorate and thyroid function, A cohort of 789 pregnant women (i.e., 396 from Cardiff, Wales; 311 from Turin, Italy; and 82 from Dublin, Ireland) with perchlorate exposure levels shows no association between urinary perchlorate levels and free T4 levels in the pregnant women as a group or in the subgroup of pregnant women with UIC <= 100 ug/L (Pearce 2007). . A cohort of 230 pregnant women (i.e., 128 from Los Angeles, California; 102 from Cordoba, Argentina) with low perchlorate exposure levels predicted by the Blount analysis to induce a reduction of tT4 shows no association between urinary perchlorate levels and free T4 levels in the pregnant women as a group or in the subgroup of pregnant women with UIC <= 100 ug/L (Pearce 2008). From the 2005 Tellez cohort study (Tellez 2005) in three Chilean cities, a reanalysis of the data identified 16 of the pregnant women had UIC <= 100 ug/L (Gibbs 2008). The reanalysis shows no association between urinary perchlorate levels and free T4 levels in this subset of pregnant women with UIC <= 100 ug/L.

Response: See response to comment ID 29078 under comment code 2200.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0653

EPA Comment ID: 28561
EPA Comment Code: 2200

Comment: The Blount et. al. studies were useful in demonstrating that although perchlorate exposure is widespread (through diet), the review of the NHANES data clearly indicated that thyroid hormone levels measured in the study were clinically normal, even in the presence of perchlorate and other goitrogens such as nitrate and thiocyanate. The Blount et. al. 2006 study did show, however, that iodine nutrition is a significant concern, especially for women of childbearing age. The conclusions concerning associations purported in Blount et. al. 2006 are problematic as the authors failed to use consistent models to derive their findings across age, sex, ethnic and other key variables. Furthermore, it is hard to lend credence to associations between thyroid hormones and perchlorate exposure that are negative in one case for women with low urinary iodine excretion while being positive for other women. As a continuous variable, one might expect to see a more or less negative value between the groups, but not a complete change in the direction of the slope for a well-defined biological process. The statistical significance reported by the authors may be a result of the iodine level instead of the perchlorate level, as low iodine would result in elevated TSH and reduced T4 levels, while higher (i.e. sufficient) iodine levels would not be expected to result in a statistical association between thyroid hormone levels and iodine or perchlorate, as demonstrated in the study.

Response: See response to comment ID 29078 under comment code 2200.

Commenter Name: Kathy Dolan
Commenter Organization: Food and Water Watch (FWW)
EPA Document ID: EPA-HQ-OW-2009-0297-0526
EPA Comment ID: 28608
EPA Comment Code: 2200

Comment: Perchlorate has been found in the drinking water supply of 35 states and the District of Columbia. Widespread human exposure to perchlorate was confirmed by the Center for Disease Control's NHANES study, which found that 100 percent of the 2,820 randomly selected study participants had detectable levels of perchlorate in their urine. And according to your request for comment notice, dated August 5, 2009, the number of people served by water contaminated with high levels of perchlorate ranges between 53.4 and 16.8 million people.

Response: Under the first Unregulated Contaminant Monitoring Rule (UCMR 1). EPA collected and analyzed drinking water occurrence data for perchlorate from 3,865 PWSs between 2001 and 2005 under the UCMR 1. The minimum reporting level (MRL) for perchlorate under the UCMR 1 was 4 µg/L. EPA found that 160 (approximately 4.1 percent) of the 3,865 PWSs that sampled and reported had at least 1 analytical detection of perchlorate (in at least 1 sampling point) at levels greater than or equal to the MRL of 4 µg/L. These 160 PWSs are located in 26 States and 2 territories. Of these 160 PWSs, 8 are systems serving 10,000 or fewer people and 152 are systems serving more than 10,000 people. These 160 systems reported 637 detections of perchlorate at levels greater than or equal to 4 µg/L, which is approximately 11.3 percent of the 5,629 samples collected by these 160 PWSs and approximately 1.9 percent of the 34,331 samples collected by all 3,865 PWSs. The average concentration of perchlorate for those samples with positive detections for perchlorate was 9.85 µg/L and the median concentration was 6.40 µg/L.

Table 1 in the final regulatory determination presents the number and percentage of PWSs that reported perchlorate at levels exceeding various threshold concentrations.

Table 2 of today's notice presents EPA's estimates of the population served by PWSs that were monitored under UCMR 1 for which the highest reported perchlorate concentration was greater than the thresholds identified in Table 1. These population estimates are for people at all life stages. EPA has determined that a NPDWR for perchlorate could reduce perchlorate exposures for these populations to levels below the potential alternative HRLs that EPA has identified as levels of public health concerns for purposes of this determination, and that such exposure reductions present a meaningful opportunity for the reduction of health risks for persons served by PWSs.

Commenter Name: Sonia Salas
Commenter Organization: Western Growers Association on behalf of several California agriculture groups
EPA Document ID: EPA-HQ-OW-2009-0297-0652
EPA Comment ID: 28682
EPA Comment Code: 2200

Comment: U.S. EPA uses the US Centers for Disease Control and Prevention's National Health and Nutrition Examination Survey (NHANES) biomonitoring dataset in concert with the FDA TDS dataset to estimate the relative proportional intake of perchlorate from both food and water sources. The NHANES data provide the best available measure of actual human exposure to perchlorate from all sources, including food and water, using urinary perchlorate concentrations from a large U.S. population cohort. The overall exposure to perchlorate from all sources based on the NHANES data is below any meaningful level of concern identified in the available scientific literature. Thus, as a fraction of total exposure, intake of perchlorate from food alone must be well below any meaningful level of concern. FDA's TDS and food sampling data, which provides an approximation of human exposure to perchlorate from food, validates this conclusion.

Recent Epidemiological Data, Including the Blount (2006) Analysis of NHANES Data, Should Not Be Used as a Basis for a New Perchlorate Regulatory Determination.

The undersigned groups support EPA's decision to base its perchlorate regulatory determination on the NAS RfD. Some have argued that the Blount (2006b) results, which show a slight correlation between perchlorate in urine and changes in thyroid hormone levels in women with sub-optimal iodine levels, should be given considerable weight in EPA's review of its preliminary regulatory determination. In fact, the Blount analysis has several limitations which necessarily impede its use in drawing conclusions regarding the health effects of perchlorate, particularly for purposes of risk assessment and regulatory decision making. Chief among these is the fact that Blount (2006b) does not establish direct causation, only an association between two independent data sets. A number of intervening factors could cause or contribute to the reported decrease in thyroid hormone levels, including methodological issues such as the use of relevant measures of thyroid function (total T4 versus free T4) and appropriate biomonitoring data (24 hour urine versus spot urine samples). Second, even if changes in thyroid hormone levels were considered adverse (they are not), the changes identified in Blount (2006b) were not outside the normal ranges for thyroid hormone levels. Third, estimated perchlorate doses based on the urinary concentrations were below the level that can

trigger inhibition of iodide uptake, the non-adverse precursor effect that is the basis of the NAS NOEL.

The Blount (2006b) results conflict with the overwhelming body of scientific evidence showing that perchlorate has no effect on the thyroid at environmentally relevant levels. Similar concerns have been raised by independent organizations such as the American Thyroid Association[FN2: The American Thyroid Association in 2007 concluded that the CDC study findings were "intriguing," but limited in their application to the setting of exposure standards. (http://www.thyroid.org/professionals/publications/statements/06_12_13_ perchlorate.html).], and a key member of the NAS perchlorate panel has indicated that the NAS RfD remains sufficiently health protective[FN3: In April 2007 - after publication of the CDC study - NAS panelist Dr. Robert Utiger, senior physician with the Harvard Institutes of Medicine, testified before Congress and stated: "I continue to believe that a reference dose of 0.007 mg/kg/day (24.5 ppb) is quite adequate."].

Response: EPA disagrees that the overwhelming body of scientific evidence showing that perchlorate has no effect on the thyroid at environmentally relevant levels. See response to comment ID 29078 under comment code 2200.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0647
EPA Comment ID: 28717
EPA Comment Code: 2200

Comment: If the association between perchlorate and thyroid hormone levels was causal, as is sometimes inferred from the Blount study, then logically the effects of thiocyanate and nitrate observed by Blount in connection with those same hormones should also be viewed as causal. If that were so, it would then appear that thiocyanate has all of a sudden become a remedy against goitrogens instead of a goitrogen itself, and nitrate would only act as a goitrogen when iodine levels were sufficient. That of course would be very surprising, and would be inconsistent with years of scientific observations and studies regarding these substances. As discussed in greater detail below, we have reviewed the information presented in the Blount study regarding perchlorate, and the full range of substances in the same NHANES 2001-2002 database, and have concluded that perchlorate is not the cause of observed TH impacts, but is simply a marker for other thyroid affecting substances.

1. The four orders of magnitude difference between the adverse effect levels found in the two most cited recent studies in relation to perchlorate, the Greer study and the Blount study

In stark contrast to all previous studies, the results of the Blount study suggest that if the relationship between perchlorate and thyroid hormones is causal, perchlorate is about 10,000 times more potent than previously found. It is simply not plausible that all other studies would have missed this surprising outcome, particularly in view of the fact that perchlorate was and still is used as a drug in the treatment of thyroid disorders.

From Blount (NHANES 2001-2002) data and regression curves, the average urinary level of 2.84 ug/L, which is found to be related to thyroid hormone (TH) change, is equivalent to an oral perchlorate dose of approximately 0.00004mg/kg- day[FN2: Blount BC, Valentin-Blasini L, Osterloh JD, Mauldin JP, Pirkle JL, 2006a. Perchlorate Exposure of the U.S. Population, 2001-2002. Journal of Exposure Science and Environmental Epidemiology, 1-8.]. This is 100 times lower than the dose of 0.004 mg/kg-day that was found in the Greer study to be without effect not even on iodide uptake and which led to the NAS RfD based on a (slightly higher) NOEL of 0.007 mg/kg-day. Further this dose of 0.004 mg/kg-day on itself is about 100 times smaller than 0.5mg/kg-day, the dose found to have no effect on THs[FN3: NAS 2005, Health Implications of Perchlorate Ingestion, The National Academies Press, Washington, DC, 2005.]. So, in stark contrast to what has been found in the body of the literature, the conclusions of the Blount study would suggest that perchlorate is about 10,000 times more potent than measured in previous studies as illustrated in fig. 3, below.

Fig. 3 [see PDF docket ID EPA-HQ-OW-2009-0297-0647]

The NAS RfD of 0.0007 mg/l has often been expressed in the media as "a couple of drops in an Olympic seized swimming pool" to make it more visually comprehensible. We could push this metaphor a bit further: the 10,000 times lower dose would then mean that the level represents a couple drops in 10,000 Olympic sized swimming pools. If the effect of perchlorate were indeed so strong, the resulting drinking water public health goal (PHG) would be well below 25/100 ppb and closer to 25/10,000 ppb or 0.0025 ppb which is at least 2 orders of magnitude below the mean natural perchlorate background in drinking water.

Finally, if the causal interpretation of the results of the Blount study are to be believed, the downstream TH adverse effect level of 0.00004 mg/kg-day would be 2 orders of magnitude lower than the upstream iodine uptake inhibition non- effect level. This is in itself contradictory, since according to NAS "a perchlorate dose that does not inhibit thyroid iodide uptake will not affect thyroid function" (ref. 2 above) and thus cannot affect TH levels.

A sudden four order of magnitude difference in effect level attributed to a well studied substance is extremely improbable. It is instead far more likely that the study's interpretations regarding the impact of low doses of perchlorate are inaccurate and should not be relied upon as a basis for regulation.

2. The cause of the TH changes in the Blount et al. study: is it another substance or an environmental pool of substances?

Response: See response to comment ID 29078 under comment code 2200.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28897
EPA Comment Code: 2200

Comment: B. Recent Studies Listed in the 2009 FR Notice

The Notice states that EPA has evaluated additional data made available since the 2005 RfD determination. In response to comments suggesting that other studies, particularly Blount et al. (2006), be used for defining a regulatory standard, EPA noted that new studies have provided important information to the scientific literature, but that it has "decided to make the regulatory determination based upon the current RfD." The papers EPA listed are summarized below. Based on these data, Greer et al. (2002) continues to provide the best scientific information to be used as the basis for EPA's perchlorate RfD risk assessment.

Most of these comments have been presented by Intertox in the past. Where appropriate, however, these summaries are updated with new information.

Blount et al. (2006)

Using the NHANES 2001-2002 data set and a cross-sectional study design, Blount et al. (2006) report measurement of urinary perchlorate, urinary iodide, serum TSH, and serum total T4 levels in men and women over the age of 12. The 2001-2002 NHANES data provide the largest group of subjects to date from which sampling data can be derived. The authors report that perchlorate levels were not associated with total T4 or TSH levels in men, but were a negative predictor of total T4 and a positive predictor of TSH in women with urinary iodine less than 100 ug/L. They report that in women with urinary iodine greater than 100 ug/L, urinary perchlorate was a positive predictor of TSH, but not associated with T4. The significance of evaluating women with urinary iodide less than 100 ug/L is based on the World Health Organization (WHO) statement that a median urinary iodine concentration for the entire population, based on spot samples of less than 100 ug/L, is indicative of overall iodine deficiency for that population (WHO, 2004).

This study has drawn a great deal of attention as it may be misinterpreted to demonstrate an "effect" of perchlorate, albeit at exposures below those that cause measurable IUI. A number of considerations, however, should be noted to better understand the significance of the data reported.

First, as stated above, ATSDR (2008) reviewed this study in their assessment and did not feel it merited any special consideration over other studies in the well developed perchlorate literature database. It states that its decision "...was made after a careful evaluation of the NRC report and of studies that have been published after the NRC (2005) report. The results from newer studies do not change the bottom-line recommendation" (ATSDR, 2008).

Second, it is important to interpret the results of scientific research based on what is known about the biological system. For example, there is a difference between "statistical significance and "clinical significance." A "statistically significant" difference simply means it is unlikely that a difference between two variables (e.g., measurements) is due to chance. With a well designed experiment, statistical significance can be extremely important. Because statistical significance is also a function of sample size, variability in the variables measured, etc., the finding of statistical significance does not necessarily mean the difference is large, important, or biologically significant. For biological data, it is important to understand whether something that is statistically significant is also clinically significant; that is, whether a change in a variable or parameter is large enough to affect a clinical or medical condition (e.g., development of hypothyroidism). Blount et al. (2006) report statistically significant relationships for some variables, but do not report any variables with clinical significance, such as free T4.

The type of study conducted by Blount and colleagues (i.e., a cross-sectional study) cannot determine causation, only association between the variables studied (Wartenberg and Buckler, 2001). If important variables are missing, then spurious conclusions can be made. Thus, without a full set of thyroid-specific variables measured, including repeated 24-hour urinary iodide measurement, any association should be examined carefully for reliability.

Furthermore, perchlorate did not actually lower (nor was it associated with) thyroid hormone levels outside the normal range of values. Assuming that it had, the NRC committee does not think that "...transient changes in serum thyroid hormones or TSH concentrations are adverse health effects; they are simply biochemical changes that might precede adverse effects" (NRC, 2005). For each individual in the NHANES study, a single spot urine sample and a single plasma sample for analysis of thyroid hormones and other parameters were collected. These data do not provide more than a "snapshot" or transient assessment of these individuals.

Regarding Blount et al. (2006), ATSDR states, "limitations of the study acknowledged by the investigators include those common to cross-sectional analyses, the assumption that urinary perchlorate correlate with levels in the thyroid stroma and tissue, and the measurement of total T4 rather than free T4" (ATSDR, 2008).

Third, any study must have careful consideration for the parameters and variables that are measured or available and how these variables relate to the outcome of interest. NHANES is designed to collect a broad range of data about the health and diet of people in the United States. NHANES collected data on some parameters relevant to thyroid function, but these parameters fall short of providing sufficient information needed to clearly understand thyroid health. Only two clinical measures of thyroid function were taken (total serum T4 and TSH). Missing where free T4, thyroid binding globulin (TBG), and T3 among others. Iodine status was reported on the basis of spot urine samples, which are neither the preferred, nor most reliable, measure of urinary iodide (Barr et al., 2005). Further, NHANES did not collect data on the incidence of autoimmune thyroiditis, the most common thyroid disorder in the U.S., which causes changes in serum T4, T3, and TSH concentrations due to errant immune mechanisms attacking the thyroid gland, called Hashimoto's thyroiditis (NRC, 2005). Intertox (2008) provides a more thorough discussion regarding the use of spot urine testing, confounders, and use of the available NHANES variables to draw conclusions.

This study did not present urinary measures normalized to creatinine, although creatinine was included as a variable in the regression analysis. The concentration of dissolved substances in urine, such as iodide, may vary between individuals or between samples from the same individual based on water intake. Normalization with creatinine is meant to normalize for dilution, not variability due to differences in exposure. It is not a perfect method, but is commonly used to account for this dilution (Furnee et al., 1994). Normalization may have been particularly useful in dividing the women up in to those with urinary iodide less than and greater than 100 ug/L.

Response: See response to comment ID 29078 under comment code 2200.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28899

EPA Comment Code: 2200

Comment: Fourth, not only were the thyroid hormone values within normal clinical ranges, but urinary perchlorate levels as a surrogate for dose demonstrate that these perchlorate exposures are well below the threshold for zero inhibition of iodide uptake, a nonadverse effect. Exposures that are below the threshold for iodine uptake inhibition are below the NOEL for perchlorate and are not adverse (NRC, 2005; Greer et al., 2002).

Finally, based on the premise that science is incremental and knowledge builds collectively over time, concerns raised by scientists related to the Blount et al. (2006) study should be considered an opportunity for further study. Furthermore, recognizing that urinary spot iodine or single point iodine measures are not a good indicator of iodine status, a different approach is being considered by Dr. Blount. More research should be conducted to better understand the results of this study.

Response: See response to comment ID 29078 under comment code 2200.

Commenter Name: Jonathan Borak
Commenter Organization: Yale School of Medicine
EPA Document ID: EPA-HQ-OW-2009-0297-0209
EPA Comment ID: 29078
EPA Comment Code: 2200

Comment: The key findings of the Blount study are well known:

1) Measures of thyroid function (T4 and TSH) were significantly associated with urinary perchlorate levels in women, but not men;

2) T4 levels were negatively associated with urinary perchlorate levels in women with spot urine iodine levels <100 ug/L, but not >=100 ug/L. TSH levels were positively associated with perchlorate in both groups of women;

3) Urinary thiocyanate levels were negatively associated with TSH in women with spot urine iodine levels >=100 ug/L, but there was no association in those with <100 ug/L. Urinary thiocyanate levels were not significantly associated with T4 in women with spot urine iodine levels <100 ug/L or >=100 ug/L;

4) Urinary nitrate levels were negatively associated with T4 in women with spot urine iodine levels >=100 ug/L, but not in those with levels <100 ug/L. Urinary nitrate levels were not significantly associated with TSH in women with spot urine iodine levels <100 ug/L or >=100 ug/L.

The Blount perchlorate findings are provocative, and at first seem biologically plausible. But when all study findings are viewed together, their pattern is inconsistent with what is generally accepted to be the basic physiology of the Sodium/Iodide Symporter (NIS).

Three principal anions, perchlorate, thiocyanate and nitrate (along with other 'lesser' anions) exert qualitatively similar effects upon the thyroid, i.e., they competitively inhibit iodine uptake by the NIS (2-5). The NIS effects of these molecules have been shown repeatedly to be similar in direction and

additive in magnitude, and their quantitative relationships have been well characterized (6-12). Accordingly, it is reasonable to expect that the effects on iodine uptake of increasing exposure to perchlorate, thiocyanate and nitrate would be directionally similar and quantitatively predictable.

That viewpoint is widely held by EPA scientists and others. Consider, for example, the views expressed in the recent report of the EPA's Office of Inspector General (OIG) (13):

"... the human body is exposed to all three NIS inhibitors concurrently and the resulting effect on the uptake of iodide by the thyroid is cumulative and indistinguishable from each other ..."

"The three NIS inhibitors (thiocyanate, nitrate, and perchlorate) exceed EPA's 'mode of action' requirement by sharing the same 'mechanism of toxicity' (i.e., simple competitive interaction) by inhibiting the uptake of iodide at the NIS..."

Likewise, Blount et al. agree that thiocyanate, nitrate, and perchlorate share activity as competitive inhibitors of iodine uptake (1):

"the ability of NIS to transport adequate amounts of iodide depends on the relative concentrations of these competing anions".

Steinmaus et al. also concur (14):

"High doses of perchlorate have been shown to competitively inhibit iodide uptake in the thyroid gland ... other agents, including nitrate in food and water and thiocyanate in food or from tobacco smoke also affect the thyroid by the same mechanism."

De Groef et al., in consideration of expected half-lives and exposure levels of these anions, concluded that the anti-thyroid effect of perchlorate was similar to, but substantially smaller than the respective effects of thiocyanate and nitrate (12):

"perchlorate accounts for less than 10% of possible thyroidal effects resulting from the exposure from drinking water; in food, its share is even negligible."

The inconsistencies in the Blount data are shown in the following table, which indicates the direction of expected effects on T4 and TSH levels resulting from increased exposure to perchlorate, thiocyanate or nitrate, and the effects on T4 and TSH levels observed in various groups as reported by Blount et al. No consistent pattern of effects is seen, and observed effects are not all consistent with expected.

Expected Effects and Reported Significant Effects on T4 and TSH from Increasing Exposure to Perchlorate, Thiocyanate and Nitrate [see table in PDF docket ID EPA-HQ-OW-2009-0297-0209]

Also surprising is the general absence of effects attributable to thiocyanate and nitrate. As emphasized in the OIG analysis, "typical human exposures" to thiocyanate and nitrate should have induced "substantially more NIS inhibition" than that caused by 13 ug/day perchlorate exposure, the 95th percentile exposure level in the Blount study (13).

Blount et al. recognized that such results were surprising:

"unexpected based on a mechanism of NIS inhibition. The explanation for this is unclear"(1).

Although various hypothetical and speculative explanations were proposed for such apparent inconsistency, I am not aware that any has actually been validated.

Steinmaus et al., in their re-analysis of the NHANES and Blount data, evaluated the impact of urinary thiocyanate levels on the associations between urinary perchlorate and thyroid function noted by Blount et al. (14). Like Blount, they found no significant effects in males and no significant effects in women with urinary iodine levels >=100 ug/L. And also like Blount, they recognized and could not explain the inconsistencies of their results. They could not explain the observed gender-specificity:

"We do not know why the effects we identified were seen only in women".

Similarly, they could not explain the absence of effects for nitrate, which "requires investigation beyond the scope of this paper". Finally, they could not explain the absence of perchlorate- and thiocyanate-related effects in women with spot urine iodine levels >=100 ug/L.

It is not known whether the inconsistent results reported in Blount and Steinmaus reflect yet-to-be-elucidated physiological relationships, heretofore unrecognized sources of confounding, or just 'bad luck' that adversely impacted the composition of the study cohort. Whichever, it is apparent that these data are not adequate to serve as the basis for regulatory rule making. There are too many inexplicable scientific uncertainties that can only be addressed by hypothetical and speculative thinking. Moreover, it is unlikely that reanalysis of the 2001-2002 NHANES data and Blount analyses can resolve these concerns, nor can the Steinmaus et al. analysis be used to validate the Blount et al study, as emphasized in the OIG report (13):

"the Steinmaus analysis does not corroborate the Blount analysis because both studies use the same NHANES 2001-2002 data set."

In summary, the Blount et al. and Steinmaus et al. studies are provocative and useful as the bases for hypothesis generating. They are not, however, adequate for hypothesis testing and their conclusions remain too speculative and uncertain to provide a sound basis for regulation.

Response: EPA has evaluated the Blount and Steinmaus papers as well as the OIG report cited by the commenter. EPA has determined that these studies and report are informative, but the Agency believes the recommendations of the NRC represent the best available peer reviewed science on which to base a regulatory determination. EPA believes the NRC appropriately based the RfD on iodide uptake inhibition to the thyroid, for the reasons discussed in its report. See further discussion of the RfD in today's Federal Register notice. With respect to effects of nitrate and thiocyanate, data do not exist at this time to permit a quantitative assessment of potential cumulative effects of perchlorate and other compounds that impact the sodium iodide symporter. However, EPA has committed to a drinking water strategy that outlines four principles to expand public health protection for drinking water (USEPA, 2010b). One of these principles is to address contaminants as groups. However, EPA does not believe that regulatory action to address perchlorate should be further delayed. Therefore, EPA intends to develop a proposed rule for perchlorate. EPA will continue to analyze the best available science in developing the proposed rule.

EPA Comment Code: 2300 Use of PBPK models from Clewell et al (2007) and Merrill et al (2005) to evaluate health effects

Response to Comment Code 2300: EPA reviewed, modified, and applied the perchlorate Physiologically-Based Pharmacokinetic (PBPK) models, which were originally developed by Merrill et al. (2005) for adults and Clewell et al. (2007) for other life stages, to estimate the iodide uptake inhibition in the thyroid for each life-stage (73 FR 60262; USEPA 2008a). Estimated ingestion rates were then used to estimate the internal dose and resulting iodide uptake inhibition for several life stages, including susceptible populations (e.g., pregnant women and their fetuses, as well as breast-fed and bottle-fed infants).

In the August 2009 notice, EPA stated that it was re-evaluating how best to incorporate the PBPK modeling analysis into its evaluation of perchlorate — if at all. The Agency sought comments on ways to use the PBPK modeling analysis to inform the regulatory determination.

Several commenters supported the use of the PBPK model to inform the regulatory determination only if the significant limitations of the current model are addressed. For example, the inability of the model to reflect iodide nutritional status was cited by commenters and three of four peer reviewers as an important limitation (USEPA, 2008d). Also, several commenters stated that the risks to breast-fed infants and young children are not adequately addressed by the model. They challenged that the modeling analysis is based on average weight infants and healthy adults, while the sensitive life stages for perchlorate include premature infants and hypothyroid women.

After further consideration of the peer review and public comments, EPA concludes that the PBPK modeling analysis, in the context of the perchlorate regulatory determination, is useful in examining which life stages are most susceptible to the effects of perchlorate. For example, the model indicates that a fetus may be seven times more sensitive to the effects of perchlorate than a pregnant woman. The model also allows for the estimation of the concentration of perchlorate in breast milk (thus breast-fed infant exposure) at various maternal perchlorate exposure levels. However, because of the stated limitations, EPA has decided the model does not directly bear on the current decision regarding the need for a NPDWR for perchlorate. EPA is continuing to evaluate whether the model could be used in setting a NPDWR for perchlorate.

Individual Comments

Commenter Name: Rebecca Downey
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1888
EPA Comment ID: 20773
EPA Comment Code: 2300

Comment: This decision has been based in large part on an unvetted, industry funded computer model. Any studies of this kind are highly suspect and must be verified by proper scientific studies.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination. This model has been extensively vetted, with publication of the

perchlorate specific model (Clewell et al. 2007) in a reputable journal. In addition, EPA has subjected the modified model to peer review and revised the model in accordance with peer reviewer recommendations.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20899
EPA Comment Code: 2300

Comment: Instead of using state of the art science and human bio-monitoring data from the Centers For Disease Control and Prevention (CDC) to assess risks, the agency employs a highly questionable, non-peer reviewed computer model developed by the discredited industry front group, the Chemical Industry Institute of Toxicology (CIIT). The choice to use a model instead of real world data was done for one reason, to make the risks from perchlorate look smaller than they really are. The model did achieve that result, but even this faulty analysis did not completely exonerate this potent thyroid toxin. In the end, this computer model predicts that 30,000 pregnant women would be exposed to perchlorate in drinking water at levels that exceed EPA's health reference level (HRL) of 15 ppb at any given time (EPA 2008).

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination. EPA acknowledges the Blount et al (CDC) analysis of effects of perchlorate on the thyroid status of women with low urinary iodide. However, the applicability of the analysis is limited by deficiencies noted by the authors. See response to comment code ID 28515 under comment code 2200.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20904
EPA Comment Code: 2300

Comment: Other noteworthy errors and flaws in this assessment include the following:

* The physiologically-based PBPK model that EPA uses in their assessment was designed by researchers who work for the CIIT, an industry funded research organization with a history of providing assessments to EPA that favor industry interests;

* The PBPK model that EPA uses in their assessment relies heavily on the flawed, industry-funded Greer study;

* EPA essentially ignores data from large, well-conducted human studies in favor of a PBPK computer model;

Response:
See response to comment code 2300 for a discussion of PBPK modeling in and considerations in this regulatory determination. EPA acknowledges the Blount et al. analysis of effects of perchlorate

on the thyroid status of women with low urinary iodide. However, the applicability of the analysis is limited by deficiencies noted by the authors. See response to comment code 28515.
See also response to comment ID 20899 under comment code 2300.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20910
EPA Comment Code: 2300

Comment: EPA relies on PBPK model that was designed by industry-funded group: EPA relies heavily on the PBPK model in their assessment; this model was designed in part by scientists who work for the CIIT, which is an industry-funded organization that is sponsored by corporations such as 3M, BASF, Dow, and ExxonMobil and trade groups such as the American Chemistry Council and the American Petroleum Institute.

The CIIT has a history of conducting assessments that result in outcomes that favor industry. In a 2008 report, the Government Accountability Office (GAO) notes that the CIIT developed a risk assessment for formaldehyde that was 2,400 times less stringent than a previous Integrated Risk Information System (IRIS) estimate (GAO 2008). The GAO report goes on to note "The decision to use the CIIT assessment in the plywood national emissions standard was controversial, and officials in EPA's National Center for Environmental Assessment said the center identified numerous problems with the CIIT estimate" (GAO 2008).

In 2004 the CIIT also published a model for the contaminant trichloroethylene (TCE) that proposed cancer risk values for TCE inhalation that were 300 times less protective than EPA's 2001 proposed values (Clewell et al. 2004). Leading EPA researchers subsequently published a critique of the CIIT's work, stating that their literature review did not present a "sufficiently current, complete, accurate, and transparent review of the pertinent literature," and concluding that the resulting model had not been adequately described or validated (Caldwell et al. 2006). EPA scientists also noted that the CIIT had failed to disclose their funding for the TCE model, and inappropriately implied that it had been funded by EPA.

In addition, EPA itself has noted errors in the CIIT PBPK model used in the perchlorate assessment, explaining in their report, "EPA evaluated the PBPK model code provided by the model authors and found minor errors in mathematical equations and computer code, as well as some inconsistencies between model code files" (EPA 2008). It is unclear why EPA relies so heavily on the CIIT generated PBPK model when the CIIT has a history of conducting industry friendly assessments, as with the formaldehyde example, and there are clear errors in the perchlorate model, as acknowledged by EPA.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination. As the commenter notes, EPA modified the model of Clewell et al. (2007) to correct minor mathematical errors and to expand the capabilities to reflect additional life stages. This work was conducted with the consent and support of the model developers. The model was previously peer reviewed and published in a reputable journal.

EPA does not believe that CIIT's work on formaldehyde or TCE is relevant to the perchlorate assessment.

EPA Comment Code: 2400 Use of EPA's PBPK model to evaluate health effects

Individual Comments

Commenter Name: Melanie A. Marty, Ph.D.
Commenter Organization: Children's Health Protection Advisory Committee
EPA Document ID: EPA-HQ-OW-2008-0692-0962
EPA Comment ID: 20417
EPA Comment Code: 2400

Comment: The Agency justifies the high MRL [sic] by a pharmacokinetic model that simulates iodine uptake inhibition in the human fetus and newborn based upon experimental data in rat pups. While the model has been validated in adult humans and rat pups, it has not been validated in infants and children. As we described in the CHPAC 2006 letter, use of the rat data to project pharmacolcinetics to human newborns is uncertain given the well known differences in the rate of development of clearance mechanisms between rodents and humans. The modeling performed by the Agency does not remove the clear concern for elevated neonatal exposure to perchlorate, well in excess of the RfD. This also represents an unorthodox use of pharmacokinetic modeling in regulatory risk assessment because once an RfD is established, it is inappropriate to use additional modeling to justify exceeding the RfD.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection
EPA Document ID: EPA-HQ-OW-2008-0692-1422
EPA Comment ID: 20433
EPA Comment Code: 2400

Comment: 4. The PBPK Model is Uncertain Especially for Iodine Insufficient Women. Instead of using the standard approach of comparing estimated doses to the RfD to determine safe drinking water levels, EPA is instead relying on physiologically-based pharmacokinetic (PBPK) modeling to predict IUI. MassDEP believes that the PBPK modeling has a number of limitations and may be less reliable. For example, the PBPK modeling does not adequately address effects in iodide insufficient populations and is very uncertain with respect to predicted breast milk perchlorate concentrations, effects on neonates and impacts during early fetal development. Empirical data on these issues is sparse, limiting model construction and evaluation. More robust uncertainty analysis and evaluation of model outputs is needed.

5. EPA Needs to Better Assess and Present PBPK Model Uncertainties. Since EPA relies heavily on the outputs of the PBPK model to predict breast milk perchlorate levels, a more thorough presentation of the model, model uncertainties and its outputs, in particular for breast milk perchlorate concentrations and neonatal exposures under differing maternal exposure scenarios is needed. This information should be provided to the public for review and comment, in addition to a

scientific peer review session. These are uncertain because the PBPK model relied on rat data for several key parameters that influence breast milk perchlorate concentrations. Furthermore, the model was only evaluated against limited human data derived from populations in Chile (Tellez et al., 2005).

6. US Data Indicates the PBPK Model May Underestimate Breast Milk Perchlorate. Due to differences in dietary iodide intake rates, which are likely to be much higher in Chile, as well as other factors, breast milk data from US populations with lower levels of iodine intake, such as from the Boston study (Pearce et al., 2007), should also be used for model evaluation. Based on the Pearce et al., study, MassDEP is concerned that the model may significantly underestimate perchlorate breast milk concentrations in US women. Table 1, compiled by MassDEP, compares observed perchlorate and iodide concentrations in breast milk and perchlorate in urine from the Chilean and Boston study populations. These data are consistent with higher dietary iodide intake levels in the Chilean populations compared to the Boston area. The US data also exhibits a higher breast milk to urine perchlorate concentration ratio compared to those observed in the Chilean study groups - a factor of 4 for the Boston data vs. a range of only 0.33 to 2 for the Chilean populations. This suggests that the Boston women, perhaps due to lower iodide intake, may have partitioned a greater fraction of perchlorate dose into breast milk than predicted by the model. This would result in even higher neonatal exposures than predicted by EPA at a maternal drinking water concentration of 15 ug/L, which as noted above, already exceeds the RfD.

[Table 1. Lactational Perchlorate and Iodide levels in Urine and Breast Milk - see PDF Docket ID EPA-HQ-OW-2008-0692-1422]

7. The PBPK Model is Deficient for Early Developmental Periods. Emerging data now indicate that thyroid hormone deficiency during early gestation causes neuronal toxicity (Sinah et al., 2008). The EPA has acknowledged that the lack of biological information during early fetal development limits the applicability of the PBPK modeling of the fetus and thus can not make meaningful predictions regarding early fetal IUI.

8. The PBPK Model Does Not Consider Other Potential Mechanisms of Toxicity. Additionally, the model only addresses iodide uptake inhibition. However, perchlorate not only inhibits iodide uptake but also promotes the discharge of endogenous iodide, which is not addressed in EPA's assessment. The thyroid gland possesses two kinds of iodide. The first is the iodide which is accumulated into the thyroid by an active transport mechanism, the so-called "transported iodide". The second source is the iodothyronins which are derived by hydrolysis from thyroglobulin and rapidly deiodinated within the gland to yield the so- called "endogenous iodide". It is believed that both iodide sources are used within the thyroid gland for the synthesis of hormones. Rosenberg et al., 1961; Isaacs et al., 1966; Greer et al., 1969 showed that perchlorate discharged endogenous iodide in animals, and Burgi et al.(1974) confirmed this phenomenon to occur in humans. Wolff (1974) has attempted to propose mechanisms by which perchlorate accomplishes the discharge of stored thyroidal iodide, but how this process affects thyrocytes upon short- and long-term exposure is not well understood and is not covered by the PKPB modeling.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Jeanne Herb

Commenter Organization: New Jersey Dept. of Environmental Protection
EPA Document ID: EPA-HQ-OW-2008-0692-1526
EPA Comment ID: 20448
EPA Comment Code: 2400

Comment: Proposed HRL of 15 ug/L for Perchlorate

In 2006, USEPA adopted an IRIS Reference Dose (RfD) of 0.7 ug/kg/day for perchlorate, based on the advice of the National Research Council (NRC) Committee to Assess the Health Implications of Perchlorate Ingestion (2005), which had been assembled at the request of USEPA.

The proposed Health Reference Level (HRL) for perchlorate of 15 ug/L was derived using exposure assumptions for a pregnant woman/fetus exposed to the RfD of 0.7 ug/kg/day with a Relative Source Contribution (RSC) factor of 0.6. In developing this HRL, USEPA assumed that the fetus is the most sensitive subpopulation, more sensitive than the infant, so that the infant can be safely exposed to much higher doses than the fetus. After deriving the HRL of 15 ug/L based on exposure of the pregnant woman/fetus, a physiologically-based pharmacokinetic (PBPK) model was used to evaluate the dose reaching the thyroid and to estimate effects on the inhibition of thyroidal iodine uptake in sensitive subpopulations exposed to 15 ug/L of perchlorate.

Insufficient information has been provided to the public about the details of the PBPK model to allow for the necessary evaluation of this approach. The proposal states that USEPA modified the published PBPK model to reflect the decreased urinary clearance of young infants and for other reasons, but the citation for this information (USEPA, 2008b) does not provide a document that is available to the public. Additionally, USEPA states that the modifications it has made to the published model have not yet been peer reviewed, and that this peer review will take place prior to finalizing the proposal. We believe that the results of the peer review should be available as part of the USEPA proposal, so that the public can consider the conclusions of the peer review as to the appropriateness of the approach used by USEPA.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination. The modifications to the Clewell (2007) model were peer reviewed and found to be sound. The peer review report can be found on EPA's website at http://water.epa.gov/drink/contaminants/unregulated/perchlorate.cfm. The major reservation expressed centers on attempting to use the model beyond its capabilities.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Dept. of Environmental Protection
EPA Document ID: EPA-HQ-OW-2008-0692-1526
EPA Comment ID: 20450
EPA Comment Code: 2400

Comment: Another matter of concern is the assumption that a 2.2% decrease in iodide uptake in 7-day old infants can be regarded as a No Effect Level (73 Fed. Reg. 60278 (October 10, 2008)) by extrapolation from the NRC panel's conclusions. The NRC based the conclusion that a 1.8% decrease was a No Effect Level on data from normal healthy adults. Additionally, the 1.8% decrease was considered to be within the normal variation expected in an experimental measurement, which differs in concept from a prediction of a decrease of any magnitude by a model. Although iodide

uptake by the thyroid in healthy infants functions at a level similar to adults, this assumption that a decrease of 2.2% is inconsequential does not provide the level of protection that is usually extended to clearly sensitive subpopulations. Critically, infants do not achieve complete maturity of thyroid function until 1-2 months postnatally, display a shorter thyroxine half-life, and do not have the same degree of thyroid reserve capacity as healthy adults (Brown et al., 2004; van den Hove et al., 1999; Zoeller and Rice, 2004). While most infants with severe thyroid problems are identified within a few days after birth, premature infants, infants with subclinical hypothyroidism or with low iodine intake are not represented by the average healthy infant considered by the PBPK model. Furthermore, the predictions for perchlorate exposure and decreases in iodide uptake are only averages for the group considered, normal healthy infants, and the range that could be predicted by the model due to differences in pharmacokinetic and pharmacodynamic factors is not given.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Robert Howd
Commenter Organization: California Environmental Protection Agency, Water Toxicology Section
EPA Document ID: EPA-HQ-OW-2008-0692-1671
EPA Comment ID: 20647
EPA Comment Code: 2400

Comment: III (A)(3), pp 60268-9. The elegant PBPK model of Clewell et al. (2007) represents a significant advance in understanding potential perchlorate effects on the human maternal/fetal unit, and the maternal to infant passage of perchlorate and iodide through mother's milk. However, some of the parameters in this model are inadequately understood and documented. The adaptations utilized by EPA (U.S. EPA, 2008) appear to improve the model, but we are concerned that it may not sufficiently address fetal and infant iodide/perchlorate ratios and potential effects on thyroid hormone regulation. We believe that more review of the model and its interpretation are needed, especially considering potential inhibition of fetal iodide uptake in mothers with low iodide consumption (i.e., maternal/fetal variation).

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Robert Howd
Commenter Organization: California Environmental Protection Agency, Water Toxicology Section
EPA Document ID: EPA-HQ-OW-2008-0692-1671
EPA Comment ID: 20650
EPA Comment Code: 2400

Comment: IV (B)(5), pp 60277-9. PBPK modeling. Critical parameters such as relative transport of iodide and perchlorate across the placenta and uptake into fetal thyroid are not yet available. We therefore would judge these calculations and conclusions very cautiously.

For estimation of infant's exposure to formula on p. 60279, the EPA has referred to their new evaluation of the data from the 1994-96 and 1998 Continuing Survey of Food Intakes by

Individuals, by Kahn and Stralka, which was recently published online in the Journal of Exposure Science and Environmental Epidemiology. We note that the values cited from this source are less than we have been using, based on EPA (2004), but we have not had the opportunity to compare the evaluations and strength of conclusions in detail.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1748
EPA Comment ID: 20654
EPA Comment Code: 2400

Comment: Third, in particular, the PBPK model referenced in the letter has already been extensively peer-reviewed. Furthermore, the EPA is conducting an independent external letter peer review of a draft report prepared by EPA's Office of Research and Development titled, Inhibition of the Sodium-Iodide Symporter by Perchlorate: An Evaluation of Lifestage Sensitivity Using Physiologically-based Pharmacokinetic (PBPK) Modeling. This review is expected to be completed shortly. The underlying model and its expansions are already the subject of four peer-reviewed, published scientific articles.[FN5: Rebecca A. Clewell et al., The Use of Physiologically-Based Models to Integrate Diverse Data Sets and Reduce Uncertainty in the Prediction of Perchlorate and Iodide Kinetics Across Life Stages and Species, Toxicol. Ind. Health, 2001, 210-222; Rebecca A. Clewell et al., Predicting Fetal Perchlorate Dose and Inhibition of Iodide Kinetics During Gestation: A Physiologically-Based Pharmacokinetic Analysis of Perchlorate and Iodide Kinetics, 2003, Toxicol. Sci., 2003, 235-55; Elaine A. Merrill et al., PBPK Model for Radioactive Iodide and Perchlorate Kinetics and Perchlorate-Induced Inhibition of Iodide Uptake in Humans, Toxicol. Sci., 2005, 25-43; Rebecca A. Clewell et al., Perchlorate and Radioiodide and Kinetics Across Life Stages in the Human: Using PBPK Models to Predict Dosimetry and Thyroid Inhibition and Sensitive Subpopulations Based on Developmental Stage, J. Toxicol. Envtl Health, 2007, 408-28.] Significantly, the NAS panel endorsed it as "the best available approach" for determining effects in sensitive subpopulations where experimentation is impossible. While we are not aware of the particular changes EPA staff made to the PBPK model for use in the preliminary determination, the Federal Register notice provides an estimate of predicted changes in iodine uptake inhibition (IUI) in sensitive subpopulations that do not differ significantly from the published findings in Clewell et al. (2007). The results of this modeling estimate that certain sensitive populations (although not the most sensitive population, which are pregnant women and their fetuses) may have exposures in excess of the RfD. However, these groups would have minimal IUI at environmental doses. These conclusions are important enough to state again: even at doses greater than the reference dose, sensitive subgroups within the population may have minimal changes in their IUIs. The magnitudes of these changes are small enough to be attributable to normal fluctuations, possibly from diet. As noted by the NAS review, unless there is a sustained and significant change in IUI, adverse effects from perchlorate will not occur.[FN6: See Note 1.]

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Caroline Baier-Anderson, PhD

Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20950
EPA Comment Code: 2400

Comment: A major concern is that the application of the PBPK model after the establishment of an RfD is a novel concept that must be thoroughly vetted prior to using in the regulatory setting. EPA should convene a peer review process to evaluate this novel use of a PBPK model, not just for use in developing a health advisory level for perchlorate, but its use in the general sense. Such deviations from the standard risk-based approaches must be thoroughly evaluated, with recommended applications and limitations clearly identified.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20968
EPA Comment Code: 2400

Comment: EPA seems to aim to limit uncertainties as much as is possible by taking into account the latest available evidence such as the NHANES data and make use of sophisticated models such as the FDA TDS and the PBPK models. This is laudable.

Response: EPA has assessed the available scientific information on health effects and exposure to perchlorate. See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20997
EPA Comment Code: 2400

Comment: 3. EPA ignores fails to adequately consider evidence that the proposed HRL is not safe

Although EPA's scientific staff issued a rigorous review of the PBPK model and its findings, the Agency has ignored the most important conclusions of the report, that infants and young children will have a perchlorate intake that exceeds the RfD. Instead, the preliminary determination seems to suggest that the PBPK model results support the Agency's proposed HRL. This is not the case.

A. The PBPK model provides evidence that at the proposed HRL, infants and young children will have a perchlorate intake that exceeds the reference dose.

The EPA scientific staff conducted a rigorous evaluation of the application of the physiologically-based pharmacokinetic (PBPK) model, particularly as it applies to sensitive life-stages.[FN49: EPA Office of Research and Development. Inhibition of the sodium-iodide symporter by perchlorate: An

evaluation of lifestage sensitivity using physiologically-based pharmacokinetic (PBPK) modeling. Preliminary Draft. October 2, 2008. EPA/600/R-08/106A. Docket ID No. EPA-HQ-OW-2008-0692-0076.] On October 2, 2008, EPA issued the report, which identifies some very troubling findings, including evidence that consuming water that was contaminated at the HRL of 15 ug/L would lead to bottle-fed infants exceeding the reference dose by 5-fold and young children exceeding the reference dose by 2.8-fold, based on average food contamination rates, average body weights, and 90th percentile water consumption rates for each age group (Staff Report, Table 4).[FN50: EPA Office of Research and Development. Inhibition of the sodium-iodide symporter by perchlorate: An evaluation of lifestage sensitivity using physiologically-based pharmacokinetic (PBPK) modeling. Preliminary Draft. October 2, 2008. EPA/600/R-08/106A. Docket ID No. EPA-HQ-OW-2008-0692-0076.] Specifically, the staff report found that the PBPK model predicted the perchlorate intake (ug/kg-day) from average food consumption, and 90th percentile water consumption held to 15 ug/L perchlorate as shown in Table 1. The table also identifies the magnitude by which the RfD is exceeded at the proposed HRL.

[Table 1: Perchlorate intake at a Health Reference Level of 15 ug/L - see PDF Docket ID EPA-HQ-OW-2008-0692-????]

These values were also reported in the Federal Register notice, Table 8.[FN51: 73 Fed. Reg. at 62078.] Note that the overwhelming majority of perchlorate for these age groups is coming from water or breast milk, and not from solid food. These data, generated from the PBPK model predictions, provide substantial scientific support for the conclusion that infants (both breast- and bottle-fed) and young children would exceed the reference dose if their dietary water were contaminated with perchlorate at the HRL.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 21001
EPA Comment Code: 2400

Comment: B. PBPK model supports an uncertainty factor of at least 15-fold

EPA normally uses a 10-fold default uncertainty factor to adjust for variations among individuals, called the intraspecies factor, when the Agency lacks adequate data to calculate intra-individual variability. EPA used this 10X intraspecies factor for its perchlorate hazard assessment on its IRIS database: "An intraspecies uncertainty factor of 10 is applied to protect the most sensitive population, the fetuses of pregnant women who might have hypothyroidism or iodide deficiency."[FN58: EPA. IRIS database. Perchlorate and perchlorate salts. http://www.epa.gov/ncea/iris/subst/1007.htm#revhis] The Agency has adopted the practice of describing the default 10-fold intraspecies factor as being comprised of the product of two 3-fold factors, one for pharmacokinetic variability, and the other for pharmacodynamic variability.[FN59: US EPA. Office of the Science Advisor: Staff Paper, Risk Assessment Principles & Practices. Page 69, Section 4.3.2. EPA/100-B-04/001. March, 2004. http://www.epa.gov/osa/pdfs/ratffinal.pdf] Pharmacokinetics describes the way that a compound such as perchlorate moves through the body,

including its absorption, distribution, metabolism and excretion. In contrast, pharmacodynamics describes what the compound does in the body, including depressing, stimulating, irritating, or killing cells or systems.

According to the IRIS glossary of terms, a PBPK model estimates the dose of a compound to a target organ or tissue by calculating the rate of absorption in the body, the distribution among target organs, the metabolism of the compound, and the excretion of the compound.[FN60: IRIS Glossary. Physiologically Based Pharmacokinetic (PBPK) Model. http://www.epa.gov/ncea/iris/help_gloss.htm#p] In other words, the PBPK model, by definition and design, estimates the pharmacokinetics of a compound.

The data from EPA's staff report however, shows that EPA's reliance on a default uncertainty factor of 10 underestimates the variability between fetuses and adults. The Executive Summary of the staff report states that "at a perchlorate dose of 7 ug/kg-day [the RfD], the percent RAIU inhibition predicted by the model for the near-term fetus is 5-fold greater than the average adult...The same analysis predicts percent RAIU inhibition approximately 1-2 fold higher for the breast-fed and bottle-fed infant (7-60 days) than for the average adult."[FN61: See EPA Staff Paper, Table 3; see also 73 Fed. Reg. 60278.] More specifically, for perchlorate, the variability between a near-term fetus (40 weeks gestation) and an adult is 5.3-fold, Therefore, the PBPK model supports a pharmacokinetic adjustment factor of at least 5-fold.

The Agency has no information from the PBPK model, or from other data, to develop an intraspecies uncertainty factor for pharmacodynamic variability, particularly between adults and sensitive lifestages. Therefore, EPA should retain a 3-fold default factor for pharmacodynamic uncertainty, consistent with its current practice.

Using the data from the PBPK model to support a pharmacokinetic intraspecies variability factor of 5, and the lack of pharmacodynamic data to support a default factor of 3, then the total intraspecies uncertainty factor should be (5 x 3) 15-fold, which is consistent with EPA policy and practices, and is supported by the available data.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination. The modeled estimates of alternative HRLs reflect only pharmacokinetics and do not consider uncertainty due to pharmacodynamics. Pharmacodynamics is dose description of the dose-dependent effect of a chemicals on the target organ. Pharmacodynamics may vary by life stage.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-2082
EPA Comment ID: 21020
EPA Comment Code: 2400

Comment: 3. Your letter also raises a concern that the PBPK model has been only validated in adult humans and rat pups, not in infants and children, adding that use of rat data to project pharmacokinetics to human newborns is uncertain given the differences in the rate of development of clearance mechanisms between rodents and humans.

PBPK modeling is the best method today to address sensitive populations when testing is not possible or ethical. In fact, the PBPK model referenced has already been extensively peer reviewed, including via modeling conducted on sensitive populations.

To be specific, the underlying model and its expansions are the subject of four peer-reviewed, published scientific articles [FN1: Rebecca A. Clewell et al., The Use of Physiologically-Based Models to Integrate Diverse Data Sets and Reduce Uncertainty in the Prediction of Perchlorate and Iodide Kinetics Across Life Stages and Species, Toxicol. Ind. Health, 2001, 210-222; Rebecca A. Clewell et al., Predicting Fetal Perchlorate Dose and Inhibition of Iodide Kinetics During Gestation: A Physiologically-Based Pharmacokinetic Analysis of Perchlorate and Iodide Kinetics, 2003, Toxicol. Sci., 2003, 235-55; Elaine A. Merrill et al., PBPK Model for Radioactive Iodide and Perchlorate Kinetics and Perchlorate-Induced Inhibition of Iodide Uptake in Humans, Toxicol. Sci., 2005, 25-43; Rebecca A. Clewell et al., Perchlorate and Radioiodide and Kinetics Across Life Stages in the Human: Using PBPK Models to Predict Dosimetry and Thyroid Inhibition and Sensitive Subpopulations Based on Developmental Stage, J. Toxicol. Envtl Health, 2007, 408-28.]. Further, EPA is conducting an independent external letter peer review of a draft report prepared by EPA's Office of Research and Development titled, Inhibition of the Sodium-Iodide Symporter by Perchlorate: An Evaluation of Lifestage Sensitivity Using Physiologically-based Pharmacokinetic (PBPK) Modeling. This review is expected to be completed shortly.

While we are not aware of the particular changes EPA staff made to the PBPK model for use in the preliminary determination, the Federal Register notice provides an estimate of predicted changes in iodine uptake inhibition (IUI) in sensitive subpopulations that do not differ significantly from the published findings in Clewell et al. (2007). The results of this modeling estimate that certain sensitive populations (although not the most sensitive population, which are pregnant women and their fetuses) may have exposures in excess of the RfD.

However, these groups would have no significant inhibition of IUI at environmental doses. These conclusions are important enough to state again: even at doses greater than the reference dose, sensitive subgroups within the population may have minimal changes in their IUIs. The magnitudes of these changes are small enough to be attributable to normal fluctuations, possibly from diet. The critical study chosen by the NAS to base its recommended RfD on, Greer et al. (2002) reported no IUI (1.8% $\pm$ 8.3) which was determined not to inhibit the first effect - a non adverse, fully reversible biochemical reaction - in the cascade of biochemical events. The PBPK modeling estimated that infants may have IUI as great as 2.2% at this dose, however, this value is well within normal variability and does not suggest that perchlorate is causing any inhibition of IUI that is different from Greer et al. (2002) and is supportive of other similar information regarding the affinity of perchlorate to the NIS.

As noted by the NAS review, unless there is a sustained and significant change in IUI, adverse effects from perchlorate will not occur.[FN2: National Academy of Sciences, Health Implications of Perchlorate Ingestion, 2005, at 165 (pdf version).]

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination. EPA agrees that the modifications to the Clewell (2007) model were peer reviewed and found to be sound. The peer review report can be found on EPA's website at http://water.epa.gov/drink/contaminants/unregulated/perchlorate.cfm.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-2082
EPA Comment ID: 21021
EPA Comment Code: 2400

Comment: 4. Also concerning PBPK Modeling, your letter suggests that EPA's application of the PBPK modeling is "unorthodox" in regulatory risk assessment because it should not be used to exceed an established RfD. However, EPA's use of the modeling is not used to exceed the RfD in this case, but rather to validate the benchmark of 15 ug/L as the HRL, and supports the point that the HRL derived by the Agency is even more health protective than the already conservative NAS-based RfD that has been adopted by EPA. EPA policy has been to use PBPK modeling for determining human equivalent exposures (HEEs) and adjusting default uncertainty factors [FN3: U.S. EPA Risk Assessment Forum, A Review of the Reference Dose and Reference Concentration Process, December 2002.] Significantly, the NAS perchlorate panel agreed with EPA in finding PBPK modeling is "the best available approach" in determining effects in sensitive populations where experimentation is impossible (NAS, 2005) [FN4: The NAS panel also concluded the following: "By applying factors for life-stage differences (such as pregnant or lactating female rat vs. adult male rat) and for species differences (such as adult rat vs. adult human or pregnant or lactating rat vs. pregnant or lactating human), one can constrain PBPK simulations by using known physiologic measures and biochemical constants to estimate HEEs in potentially sensitive populations that may not be suitable for experimental validation."] EPA personnel have co-authored studies involving PBPK modeling and perchlorate (Merrill et al., 2005) and present for this preliminary determination, a model from Clewell et al. (2007) that was modified by making coding changes which served to improve the predictability of the model and therefore its overall usefulness. With this modified model, EPA is able to predict doses and changes in RAIU in pregnant women, fetuses, infants, and young children.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination. See response to comment code 5220 for a discussion of alternative health reference levels. The modifications to the Clewell (2007) model were peer reviewed and found to be sound. The peer review report can be found on EPA's website at http://water.epa.gov/drink/contaminants/unregulated/perchlorate.cfm.

EPA agrees that significant uncertainty in risk estimates remains whether or not the PBPK model is used. However, trading one uncertain estimation technique for another does not reflect progress unless the change sheds light on significant sources of uncertainty in the risk estimate. Given the incomplete nature of the PBPK model, i.e., the lack of representation of pharmacodynamics and differential life stage impact, and incomplete representation of pharmacokinetics, evaluating differential uncertainty between traditional approaches and the PBPK model referenced in the October 2008 FRN appears to have limited if any value.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21053

EPA Comment Code: 2400

Comment: 2. Perchlorate and Human Health in 2008: The EPA Preliminary Determination. These comments include two sections. The first relates to scientific policy issues. Particular focus is placed on pharmacodynamic (PBPK) modeling. Several reports in the general circulation press have suggested incorrectly that PBK modeling is unfamiliar in perchlorate risk assessment. These comments document that the PBPK modeling has been recognized by EPA and endorsed by the NAS for its effectiveness in reducing scientific uncertainty.

These comments conclude with a review of the statutory criteria establishing EPA's authority in this proceeding. Citing the NAS report as well as subsequent studies, the comments demonstrate that the Agency is correct that none of the three criteria required for setting an NPDWR are met in this case.

Thank you for the opportunity to comment on these important issues. Please do not hesitate to contact me or Dr. Richard C. Pleus, if we can provide additional information or perspective in your deliberations.

Sincerely, Michael Girard Chairman, Perchlorate Study Group

Response: The commenter is correct that application of PBPK modeling to EPA risk assessments is increasing, and that it has the potential to inform estimation of adverse effects and dosimetry across a broad range of questions. See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21100
EPA Comment Code: 2400

Comment: VII. The Published, Peer-Reviewed PBPK Model is Part of the Best Available Science EPA Can Use for the Determination

One uncertainty in the derivation of the HRL as well as in the literature database is the lack of studies that measure radioactive iodine uptake (RAIU) in the sensitive population, pregnant women and the developing fetus. Obviously, it would be unethical to conduct such as study. However, Physiologically Based Pharmacokinetic (PBPK) modeling has been found to be useful in reducing uncertainty and in filling scientific gaps in human health data on a substance. EPA policy has been to use PBPK modeling for determining human equivalent exposures (HEEs) and adjusting default uncertainty factors.[FN5: U.S. EPA Risk Assessment Forum, A Review of the Reference Dose and Reference Concentration Process, December 2002.] The NAS perchlorate panel agreed with EPA in finding PBPK modeling is "the best available approach" in determining HEEs (NAS, 2005).[FN6: The NAS panel also concluded the following: "By applying factors for life-stage differences (such as pregnant or lactating female rat vx adult male rat) and for species differences (such as adult rat vs adult human or pregnant or lactating rat vs pregnant or lactating human), one can constrain PBPK simulations by using known physiologic measures and biochemical constants to estimate HEEs in potentially sensitive populations that may not be suitable for experimental validation."] EPA personnel have co-authored studies involving PBPK modeling and perchlorate (Merrill et al., 2005)

and present for this preliminary determination, a model from Clewell et al. (2007) that was modified by making coding changes which served to improve the predictability of the model and therefore its overall usefulness. With this modified model, EPA is able to predict doses and changes in RAIU in pregnant women, fetuses, infants, and young children.

[Text Box: The utility of PBPK modeling has been previously recognized by EPA and has been endorsed by the NAS for use in reducing scientific uncertainty.]

Using a 90th percentile water intake and based on data specifically for a pregnant woman, the model predicted that,

...the pregnant woman's dose of perchlorate would not exceed the reference dose if she consumed drinking water with a concentration of 15 ug/L or less, which is consistent with the derivation of the HRL from the reference dose, but based on average body weight, 90th percentile water consumption, and 90th percentile food exposure for pregnant women. (73 FR 60280)

The model verified that exposures to 15 ppb of perchlorate in drinking water will not reduce RAIU significantly, even assuming concurrent exposure through food and water intake in the 90th percentile. This combination of high-end exposure assumption is highly unlikely, probably at the extreme end of the population distribution. For this hypothetical pregnant woman, the percent RAIU inhibition was 1.1%. The greatest inhibition was seen in 7 day old infants at 2.2%. These percent inhibitions are consistent with the 1.8% inhibition of iodine uptake from the Greer et al. (2002) No Observed Effect Level (NOEL). In fact, although 2.2% is greater than 1.8% found in Greer et al., (2002), it is well within the standard error from Greer et al. (2002) of 8.3% and would still constitute a NOEL. The NAS report noted that "the very small 1.8% decrease in thyroid radioiodide uptake identified in Greer was well within the normal variation, and therefore 1.8% IUI does not define the limit beyond which adverse effects occurs has has been incorrectly argued. The PBPK modeling is in accord with results from other corroborative studies, such as Tellez et al. (2005), which show no adverse effect on sensitive populations.

In summary, EPA's PBPK modeling supports the point that the HRL derived by the agency is even more health protective than the already conservative NAS-based RfD that has been adopted by EPA. The modeling provides scientific support that incorporating an additional level of conservatism in deriving an HRL is unnecessary as the RfD is already very conservative; based on this support, a National Primary Drinking Water Regulation would not provide a meaningful reduction in risk.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination. .

The commenter is correct that application of PBPK modeling to EPA risk assessments is increasing, and that it has the potential to inform estimation of adverse effects and dosimetry across a broad range of questions. EPA also agrees that the modifications to the Clewell (2007) model were peer reviewed and found to be sound. The peer review report can be found on EPA's website at http://water.epa.gov/drink/contaminants/unregulated/perchlorate.cfm.

Commenter Name: Mark S. Mayer

Commenter Organization: South Dakota Department of Environment & Natural Resources (DENR)
EPA Document ID: EPA-HQ-OW-2009-0297-0467
EPA Comment ID: 28481
EPA Comment Code: 2400

Comment: Specific Comments Requested by EPA:

- Comments on Use of Physiologically-Based Pharmacokinetic Model - South Dakota DENR does not have toxicologists and health effect/risk analysis experts on staff to make our own regulatory determinations for contaminant levels, but instead relies upon EPA to establish contaminant levels that are supported by a strong scientific basis and cost effective health benefits.

Response: The Safe Drinking Water Act requires EPA to use the best available, peer reviewed science in support of its decision. EPA will adhere to this requirement developing a proposed national primary drinking water regulation including a health risk reduction cost analysis.

Commenter Name: James D. Taft
Commenter Organization: Association of State Drinking Water Administrators
EPA Document ID: EPA-HQ-OW-2009-0297-0525
EPA Comment ID: 28497
EPA Comment Code: 2400

Comment: ASDWA Responses to Specific Requests for

Comment:

Comments on Use of the Physiologically-Based Pharmacokinetic Model (PBPK) - ASDWA does not have any detailed comments to offer on the use of the PBPK model to evaluate or predict the health impact of perchlorate or about how this information could support a regulatory determination. State drinking water programs, with a few exceptions, do not have toxicologists or other health effect and risk analysis experts on their staffs to provide detailed evaluations of these issues. That is why very few states adopt their own regulatory standards but rely on EPA to set appropriate Maximum Contaminant Levels (MCLs). As stated earlier, ASDWA expects EPA to use sound scientific data from peer reviewed research to make regulatory determinations. States must explain to water systems and the public how the resulting MCLs protect public health and a strong scientific basis for the rule makes that justification credible. We do appreciate the rigor with which the Agency has explored this issue and the range of options being considered in connection with the PBPK model as well as the evaluation of the relative sensitivity of the various life stages to perchlorate exposure in drinking water.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Shannon Cunniff
Commenter Organization: Department of Defense (DOD)
EPA Document ID: EPA-HQ-OW-2009-0297-0411
EPA Comment ID: 28521

EPA Comment Code: 2400

Comment: Comment No. 4

Section III. 2. What Were the Key Scientific Issues Raised by Commenters

Page & Paragraph Page 41885 Col 1, Para 4 Col 2, Para 2

Comment EPA has issued several PBPK guidance documents, including Use of Physiologically Based Pharmacokinetic Models to Quantify the Impact of Human Age and Interindividual Differences in Physiology and Biochemistry Pertinent to Risk (EPA/600/R-06/014A) and Approaches for the Application of Physiologically Based Pharmacokinetic Models and Supporting Data in Risk Assessment (EPA/600/R-05/043F), and notes at its National Center for Environmental Assessment webpage (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=2044, accessed 15 September 2009), "Physiologically-based pharmacokinetic (PBPK) models have increasingly been employed in chemical health risk assessments carried out by the U.S. Environmental Protection Agency (EPA), and it is anticipated that their use will continue to increase." Given such activities and statements, it is not clear from the current notice, why the agency is now proposing removing the PBPK models from the evaluation of life-stage specific differences in susceptibility. In fact no reasons are given, other than a few commenter concerns about (1) the level of peer review and (2) the existence of uncertainty in the model parameters, neither of which provide a sound reason for discarding the models. This is particularly troubling given that EPA specifically released its final, peer-reviewed report on Inhibition of the Sodium-Iodide Symporter by Perchlorate: An Evaluation of Life Stage Sensitivity Using Physiologically Based Pharmacokinetic (PBPK) Modeling (EPA/600/R-08/106A) as supporting material for the19 August 2009 Federal Register notice (accessed on 15 September 2009 at the NCEA webpage http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=212508#Download). In the document, EPA definitively concludes that with minor modifications proposed by the Agency the Clewell et al. (2007) and Merrill et al. (2005) PBPK models are acceptable to calculate the life stage differences in the degree of thyroidal NIS RAIU inhibition at a given level of perchlorate exposure.

Suggested Action, Revision and References (if necessary) It is recommended that the PBPK models continue to be used in the evaluation of perchlorate life- stage susceptibility.

Category* S. M

Comment No. 5

Section III. 2. What Were the Key Scientific Issues Raised by Commenters

Page & Paragraph Page 41885 Col 1, Para 4

Comment The current documentation of the background for the development of the HRL gives significant weight to public comments regarding peer review of the models, which together with the lack of EPA response, gives the impression that the models have, in fact, escaped rigorous peer review. The background documentation suggests that peer review has been limited to eight experts and this is not the case.

Suggested Action, Revision and References (if necessary) It is recommended that the peer review of the models be appropriately documented. The PBPK models have undergone thorough, rigorous review by a variety of scientific panels comprised of experts from academia, regulatory agencies, the National Academies of Science, and independent consultants. Changes made to the original models by the EPA were independently reviewed by a panel of experts and deemed appropriate. Furthermore, while areas for improvement have been identified in each of the peer reviews, comments by the panels have always been positive and supportive of their intended use in identifying the susceptible life-stages for perchlorate inhibition.

Category* E, M

Comment No. 6

Section III. 2. What Were the Key Scientific Issues Raised by Commenters

Page & Paragraph Page 41885 Col 2, Para 2

Comment As suggested in EPA (2009), there are indeed uncertainties in some of the model parameters, as there is always uncertainty in any calculation of risk. The benefit of using PBPK models is that the uncertainty in the calculations is more transparent than the typical default approach. For example, it is clear from evaluation of the model output that there is not enough data to adequately define exposure parameters (particularly in the young neonate) and urinary clearance parameters. By focusing on those model parameters with uncertainty, collection of the data needed to improve our knowledge and reduce uncertainty can be initiated. Furthermore, the effect of these model parameters on the predictions of inhibition can be explored. The fact that the overall predictions of inhibition across life-stages were not significantly changed despite the changes made to the model intake and clearance parameters by the EPA indicates that the models are robust within the potential range of parameters made available in the data. The models help to define and decrease the areas of uncertainty, rather than increase them, which is what happens when the models are removed from consideration and life-stage comparisons are made solely on estimates of average of upper bound estimate of food and water intake.

Suggested Action, Revision and References (if necessary) It is recommended that the PBPK models be utilized and the uncertainty analysis be performed appropriately.

Category* S. M

Comment No. 7

Section III. 2. What Were the Key Scientific Issues Raised by Commenters

Page & Paragraph Page 41885 Col 2, Para 2

Comment Some of the uncertainty can be addressed through the use mathematical and statistical tools to estimate the effect of the parameter variability on model predictions. Using statistical tools such as Monte Carlo analysis, we can determine ranges of inhibition expected at proposed HRLs while taking into account variability in the parameters. Without the models, the uncertainty still exists. There is still a lack of data for exposure and clearance in the HRL approach but it is not as

obvious. Discarding the models does not eliminate uncertainty in lifestage dosimetry, but it is hidden within the additional uncertainty associated with the default calculations. Reverting to the default approach based on external exposure concentrations in media, does not improve the estimate of risk or increase the likelihood of protecting the public. Rather it allows the risk assessment to be driven by the data that is most readily available and easiest to explain than trying to deal with the more difficult task of incorporating the best available science. We do view this approach as scientifically defensible.

Suggested Action, Revision and References (if necessary) It is recommended that the PBPK models be utilized and the uncertainty analysis be performed appropriately.

Category* S. M

Comment No. 8

Section III. 2. What Were the Key Scientific Issues Raised by Commenters

Page & Paragraph Page 41885 Col 2, Para 2

Comment The approach previously proposed for using the models to evaluate life-stage specific susceptibility to iodide uptake inhibition was a reasonable use of the models. They were not used to derive the HRL, but were used to verify that the recommended HRL was protective of all life-stages. Public comments and the subsequent revised proposal appear to imply that the previous calculations were performed using the PBPK models. This is not the case. According to the EPA (2008), the models were run to provide a second, independent test for the adequacy of the proposed HRL. This analysis was thoughtful, novel and informative to the level of risk associated with the proposed HRL. It is not clear why this approach was not followed in the current assessment, particularly in light of the subsequent completion and positive result of the PBPK model peer review.

Suggested Action, Revision and References (if necessary) It is recommended that the PBPK models be used in a reasonable approach.

Category* S. M.

Comment No.

Section III.A. 4. Request for Comment on Alternative Approaches. a., b., c.

Page & Paragraph Page 41886

Comment Clarity needs to be improved relative to presentation of the PBPK model results.

It also would be helpful if the uncertainties associated with the various alternative options, such as use of PBPK model (e.g., iodide status, and other data deficiencies) were compared with other suggested methods for developing health risk levels (e.g., using human data available from "direct measurement") in a tabular format, to help improve the clarity of the benefits/drawbacks of the alternative processes. For example, uncertainty was linked to the modeling code, the availability of data for the many variable parameters in the model, the combination and handling of the data

selected for use in simulations, and, in particular, the previous lack of human data for specific life stages including pregnant women and their fetuses, lactating women and their babies, and bottle-fed infants for which rat data were adapted. The inability of the model to reflect iodide nutritional status also was cited by three peer reviewers as an important limitation. Recent and available "direct measurement" data, as cited here, for sensitive lifestages should be evaluated for potential use in reducing these identified areas of uncertainty. This would also help identify areas for potential future research.

Suggested Action, Revision and References (if necessary) We recommend a tabular format of changes made to the EPA PBPK model in its last revision (May 2009) and the impact of those changes.

We recommend a tabular comparison of the impact on thyroid hormone levels from recent human data for perchlorate, thiocyanate, nitrate and iodide in healthy populations and additional modeling of these data to help determine the impact of low iodide for sensitive subpopulations, such as pregnant women and infants.

Category* E

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

The commenter is correct that application of PBPK modeling to EPA risk assessments is increasing, and that it has the potential to inform estimation of adverse effects and dosimetry across a broad range of questions. EPA also agrees that the modifications to the Clewell (2007) model were peer reviewed and found to be sound. The peer review report can be found on EPA's website at http://water.epa.gov/drink/contaminants/unregulated/perchlorate.cfm. However, the major reservation expressed was with the use of the model, not the validity of the internal calculations. EPA believes that the tabular comparison recommended above is an interesting approach that should be considered at such time as sufficient data to conduct a cumulative assessment for chemicals affecting the NIS receptor become available.

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 28744
EPA Comment Code: 2400

Comment: The NDEP recommends that the EPA incorporate the following key concepts into the decision-making process, as explained more fully in the attached comments:

1. Additional clinical data are needed to help refine the PBPK model. Data are needed for adults, including pregnant women, and for neonates concerning thyroidal iodine capacity and the effects of sodium-iodide symporter (NIS) upregulation on thyroidal iodine uptake and/or thyroxine levels. Also, additional studies of other adults are needed to evaluate the effects of temporary iodine deficiency and NIS upregulation on perchlorate competitive inhibition of thyroidal iodine uptake and/or free thyroid hormone levels. This additional research would provide useful data to consider

in further refining the PBPK model to accurately reflect the effects of iodine deficiency in pregnant women, fetuses and neonates.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination. EPA plans to continue to evaluate the best available science on perchlorate in preparing a proposed maximum contaminant level and goal for perchlorate.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28798
EPA Comment Code: 2400

Comment: REQUEST FOR COMMENTS ON ALTERNATIVE APPROACHES

a. Using the PBPK model to evaluate the relative sensitivity of life stages to perchlorate exposure in drinking water

NRDC Response: The PBPK model can be used to evaluate life stage sensitivity, and it provides evidence that at the proposed HRL of 15 ppb, infants and young children will have a perchlorate intake that exceeds the reference dose.

The EPA scientific staff evaluated the application of the PBPK model, particularly as it applies to sensitive life-stages.[FN26: EPA Office of Research and Development. Inhibition of the sodium-iodide symporter by perchlorate: An evaluation of lifestage sensitivity using physiologically-based pharmacokinetic (PBPK) modeling. Preliminary Draft. October 2, 2008. EPA/600/R-08/106A. Docket ID No. EPA-HQ-OW-2008-0692-0076] On October 2, 2008, EPA issued the staff report on this evaluation, which identifies some very troubling findings, including evidence that consuming water contaminated at the HRL of 15 ug/L (or ppb) would lead to bottle-fed infants exceeding the RfD by 5- fold and young children exceeding the RfD by 2.8-fold, based on average food contamination rates, average body weights, and 90th percentile water consumption rates for each age group.[FN27: EPA Office of Research and Development. Inhibition of the sodium-iodide symporter by perchlorate: An evaluation of lifestage sensitivity using physiologically-based pharmacokinetic (PBPK) modeling. Preliminary Draft. Table 4. October 2, 2008. EPA/600/R-08/106A. Docket ID No. EPA-HQ-OW-2008- 0692-0076.] Specifically, the PBPK model predicts that the RfD is exceeded for infants and children at the originally proposed HRL of 15 ppb, at 90th percentile water intake. (See Table 1 below). The table also identifies the magnitude by which the RfD is exceeded at EPA's originally proposed HRL of 15 ppb.

Table 1: Perchlorate intake from water at 15 ppb, with and without food intake, at 90th percentile water intake (L/day) [See PDF docket ID EPA-HQ- OW-2009-0297-0412]

These perchlorate intake values were also reported in the October 10, 2008 FR notice in Table 8.[FN29: 73 Fed. Reg. at 62078.] Note that the overwhelming majority of perchlorate for these age groups comes from water or breast milk, and not from solid food. These data, generated from the PBPK model predictions, provide substantial scientific support for the conclusion that infants (both breast- and bottle-fed) and young children would exceed the RfD if their dietary water were contaminated with perchlorate at the originally proposed HRL of 15 ppb.

Despite these conclusions, EPA announced its preliminary determination not to regulate perchlorate in drinking water. Although that FR notice did report the staff conclusions, it contradicted them by concluding that "EPA believes drinking water with perchlorate concentrations at or below the HRL of 15 ug/L is protective of all subpopulations."[FN30: Id. at 60280] EPA failed to provide any data to support its conclusion, which is contradicted by the results of PBPK modeling as reported by staff experts and in the preliminary determination.[FN31: EPA Office of Research and Development. Inhibition of the sodium-iodide symporter by perchlorate: An evaluation of lifestage sensitivity using physiologically-based pharmacokinetic (PBPK) modeling. Preliminary Draft. October 2, 2008. EPA/600/R-08/106A. Docket ID No. EPA-HQ-OW-2008-0692-0076.]

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination. See response to comment code 5220 for a discussion of alternative health reference levels.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection (MassDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0495
EPA Comment ID: 28860
EPA Comment Code: 2400

Comment: Section III Alternative Approaches to Analyzing Scientific Data Related to Perchlorate in Drinking Water

For a number of reasons we do not believe that sodium iodide symporter (NIS) inhibition predictions based on Physiologically-Based Pharmacokinetic (PBPK) modeling should, at this time, be relied upon to establish or justify a perchlorate reference dose (RfD) nor to evaluate relative sensitivities between life-stages. Although the PBPK model previously relied upon, but now under reconsideration by EPA, provides a valuable exploratory research tool and is a potentially useful predictor of perchlorate distribution and NIS effects in the adult, it is highly uncertain regarding the fetal and neonatal life-stages of most concern and may not reflect perchlorate effects on thyroid function. Our view on this issue is based on the following observations:

1) In response to peer review comments on the PBPK models, EPA noted that "the models have not been specifically parameterized to describe hypothyroid or iodine deficient individuals." In other words the model does not take into account responses in those with insufficient iodine intakes, the very group of most concern with respect to perchlorate exposures. In other documents EPA has also noted that the PBPK model did not account for within group variability in pharmacokinetics; uncertainty in several model parameters, including fetal and neonatal values derived from rodent models, and differences in adaptive responses. Although peer reviewer comments recommended that a much more robust uncertainty analysis be preformed on the model, EPA concluded that this was beyond the scope of the current effort and would be difficult to conduct due to data gaps. However, such an assessment is critical to determining the ultimate usefulness of the model predictions.

2) The perchlorate associated thyroid hormone alterations reported in Blount et al. 2006 and Steinmaus et al. 2007 in women with urinary iodine < 100 ug/L highlight some of these uncertainties, as they suggest that either the model estimates of iodide uptake inhibition (IUI) at low

perchlorate intake levels are inaccurate; that unexpectedly small increments in IUI may cause thyroid effects; and/or that perchlorate may act through additional mechanisms not captured in current models. Although NIS inhibition has been viewed as perchlorate's primary mode of action, other possible mechanisms that could contribute to its toxicity have been suggested. Based on a biologically-based dose response model of the hypothalamus-pituitary-thyroid axis and PBPK modeled perchlorate distribution and inhibition of thyroid iodide uptake, a recent assessment concluded that IUI was insufficient to explain observed changes in rat thyroid hormone levels attributable to perchlorate (McLanahan et al. 2009). These results suggest either that an additional mechanism of action exists, perhaps attributable to perchorate uptake into the thyroid and interference with other targets involved in hormone synthesis and release or that the PBPK modeling is inaccurate.

3) Although the impact of thyroid toxicants on the fetus can be buffered by the thyroid hormone synthesis and reserve capacities of the mother, iodide insufficiency and pregnancy-related stresses on maternal thyroid function increase the potential for perchlorate effects during fetal development (Glinoer 2001; Ginsberg et al. 2007). These are factors that the PBPK modeling does not adequately account for and could lead to a significant underestimate of NIS inhibition.

4) Available data indicate that neonatal exposures to perchlorate in breast milk are significant. The median perchlorate exposure to two week old nursing infants in the U.S. was predicted to be 0.206 ug/kg/day (95th percentile = 0.744 ug/kg/day) (Ginsberg et al. 2007). Other data indicate that nursing infant perchlorate exposures in the U.S. can be even higher. Based on a breast milk intake rate of 0.172 L/kg/day and reported median breast milk perchlorate concentrations (Kirk et al. 2005 and 2007; Pearce et al. 2007a), we estimate that nursing infant perchlorate intakes in three U.S. cohorts ranged from 0.56 to 1.57 ug/kg/day. Dasgupta et al. (2008) estimated breast milk perchlorate intake rates ranging from 0.3-2.1 ug/kg/day, with intakes of 9 of 13 infants exceeding the National Research Council's (NRC) RfD (NRC 2005) (Dasgupta et al. 2008).

Due to the significance of this exposure pathway, PBPK modeled estimates of perchlorate and iodide concentrations in breast milk warrant close scrutiny and additional validation. In response to peer review comments, EPA added section 4.1.1 to the May 2009 report, "Inhibition Of The Sodium-Iodide Symporter By Perchlorate: An Evaluation Of Life Stage Sensitivity Using Physiologically Based Pharmacokinetic (PBPK) Modeling." This section includes several informative comparisons of model predictions with published data but no comparison of predicted human breast milk perchlorate concentrations with published data. A comparison of breast milk data from Pearce et al 2007; Kirk et al 2005 and 2007 etc. combined with estimated US median perchlorate intakes (Blount et al 2006) should be completed, as this would provide important insight into model uncertainty regarding this critical exposure pathway.

Response: See response to comment ID 28923 under comment code 2400.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28868
EPA Comment Code: 2400

Comment: COMMENTS IN RESPONSE TO THE EPA NOTICE: ENVIRONMENTAL PROTECTION AGENCY [EPA-HQ-OW-2009-0297; FRL-8943-9] RIN 2040-AF08 DRINKING WATER: PERCHLORATE SUPPLEMENTAL REQUEST FOR COMMENTS

Prepared for: PERCHLORATE STUDY GROUP

October 8, 2009

Intertox, Inc. 600 Stewart St. Suite 1101 Seattle, WA 98101 206.443.2115 phone 206.443.2117 facsimile

TABLE OF CONTENTS

APPENDICES

LIST OF FIGURES

EXECUTIVE SUMMARY

On August 19, 2009, the Environmental Protection Agency (EPA) issued a Federal Register (FR) notice requesting comments on alternative approaches to analyzing data related to EPA's perchlorate regulatory determination (the Notice; U.S. EPA, 2009b). The Notice says that "these additional comments are sought in an effort to ensure consideration of all the potential options for evaluating whether there is a meaningful opportunity for human health risk reduction of perchlorate through a national primary drinking water rule."

The following four points summarize the response prepared by Intertox on behalf of the Perchlorate Study Group (PSG).

1. Interpretation of physiologically-based pharmacokinetic (PBPK) modeling: The use of scientifically derived PBPK models is the best scientific approach among all alternatives for evaluating the relative sensitivity of different life stages, consistent with the conclusions of EPA's peer reviewers and the National Academy of Sciences National Research Council (NRC). The current EPA PBPK model for perchlorate, however, uses values for some key parameters (e.g., urinary clearance) that are not supported by the scientific evidence. The model also does not account for up-regulation of the sodium iodide symporter (NIS). As a result, the model does not provide the best scientific estimates of iodide uptake inhibition (IUI) that would be associated with a particular perchlorate dose, and likely overestimates IUI from perchlorate exposure for various life stages. Further, input parameters are not selected from consistent points within their distributions, such that it is unclear whether the model output represents low, average, or upper-bound estimates of possible IUI. Nonetheless, the predicted levels of IUI in the Notice are low and would be indistinguishable from fluctuations resulting from differences in diet and feeding styles. No adverse health concern at any life stage would be expected based on exposure to perchlorate at the point of departure dose (7 ug/kg-d). EPA should revise this model to represent science-based accurate information on PBPK parameters and use the results to determine whether regulation is necessary.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28880
EPA Comment Code: 2400

Comment: A Interpretation of the Physiologically Based Pharmacokinetic (PBPK) Modeling

Properly conducted, PBPK models provide accurate, peer reviewed scientific information to reduce uncertainty about sensitive life stages. PBPK models for perchlorate have been under development for a number of years. In its 2005 assessment of perchlorate, the NRC identified several subpopulations that are potentially more sensitive than average adults to thyroid effects from perchlorate exposure, including pregnant women, fetuses, and infants, based in part on perchlorate PBPK models for pregnant and lactating rats and rat pups and adult humans. After the NRC evaluation, the perchlorate PBPK model was improved to include pregnant women, the fetus, lactating women, and the neonate, and was published in the peer reviewed literature (Merrill et al., 2005; Clewell et al., 2007).

Regarding the preliminary regulatory determination for perchlorate, EPA evaluated published PBPK models for perchlorate "based on their ability to provide additional information surrounding this critical effect for potentially sensitive subgroups and reduce some of the uncertainty regarding the relative sensitivities of these subgroups" (U.S. EPA, 2008a). EPA used public comments on the preliminary regulatory determination, as well as comments from an external peer review (Eastern Research Group, 2008), to further refine the model which is based on both pharmacokinetics and pharmacodynamics (U.S. EPA, 2009a) and used it to predict the relative RAIU inhibition for 17 distinct populations or life stages, including pregnant and lactating women, the fetus, and the neonate, assumed to be exposed to 0.007 mg/kg-d in drinking water. The results of this evaluation are presented in Table 1 of the Notice. From these results, EPA concluded that "by protecting the

fetus of the hypothyroid or iodide-deficient woman from the effects of perchlorate on the thyroid, all other life stages and subgroups would be protected."

EPA requested comments on three general questions regarding its use of the PBPK model as an alternative approach to assessing the relative sensitivity of different exposure populations. Responses to these questions follow. Note that the responses to Questions 1 and 2 are combined, as the questions are not substantively different.

1. EPA requests comment on using the PBPK model to evaluate the relative sensitivity of the various life stages to perchlorate exposure in drinking water.

2. EPA requests comment on the utility of the PBPK model for predicting the impact of different perchlorate drinking water concentrations on sensitive life stages to inform HRL selection.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.EPA does not agree that the model used in the 2008 preliminary determination reflects both pharmacokinetics and pharmacodynamics. The model reflects a subset of pharmacokinetic parameters for various life stages. Pharmacodynamics is dose description of the dose-dependent effect of a chemicals on the target organ. Pharmacodynamics may vary by life stage. The model depends upon the current RfD as an expression of the adverse effects of perchlorate, and any expression of pharmacodynamic variability is limited to some portion of the 10X uncertainty factor for intraspecies variability. The RfD was developed using data from adults, none of whom were pregnant. As such, it cannot reflect the potential variability among life stages due to pharamacodynamics. Data do not exist to describe the pharmacodynamic variability among life stages for perchlorate.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28881
EPA Comment Code: 2400

Comment: PBPK modeling is valuable as it can integrate dozens of experimentally derived variables drawn from peer reviewed scientific studies to characterize chemical absorption, distribution, metabolism, excretion, and toxicity/effect. PBPK modeling is well established in the pharmacological and toxicological sciences, where it has been used for more than 80 years to understand the action of chemicals in the body. More recently, PBPK models have been used in filling scientific gaps in human health data, especially when conducting animal studies is infeasible, unethical, or impractical.

As stated by Mager et al. (2003) in a review of the use of PBPK models:

The resolution of PK/PD [pharmacokinetic/pharmacodynamic] models and parameters is best achieved by having relevant pharmacokinetics..., an understanding of the mechanism of action of the drug, appreciating the determinants of any time dependence in responses, and collecting a suitable array of experimental measurements as a function of dose and time. When possible, such measurements should be sensitive, gradual, quantitative, reproducible, and meaningful.

This statement reflects scientific consensus about how scientific information should be used in a PBPK model. The EPA PBPK model is for the most part based on this philosophy and can be useful for informing risk management decisions. Not all parameters in this model, however, meet the criteria required for robust and predictive PBPK modeling. To be useful, the PBPK model inputs should be transparent and scientifically based. This would advance the overarching science policy articulated by the current EPA Administrator, Hon. Lisa Jackson.[FN8: EPA Administrator Lisa Jackson, in her May 9, 2009 memorandum on scientific integrity stated, "While the laws that EPA implements leave room for policy judgments, the scientific findings on which these judgments are based should be arrived at independently using well-established scientific methods, including peer review, to assure rigor, accuracy, and impartiality. This means that policymakers must respect the expertise and independence of the Agency's career scientists and independent advisors while insisting that the Agency's scientific processes meet the highest standards of rigor, quality, and integrity" (http://www.epa.gov/Administrator/scientificmemo.html)]

While supportive of a science based PPBK model, an evaluation of the EPA PBPK model reveals that model does not produce the best and most scientific estimates of IUI. For example, some components of EPA's PBPK model for perchlorate are not supported by the scientific literature and result in IUI predictions that do not reflect best scientific estimates of IUI associated with a particular perchlorate dose. In particular, EPA's uses values for one of the key parameters in the PBPK model, the urinary clearance of perchlorate, that are not supported by the scientific literature.[FN9: Per EPA's evaluations, perchlorate PBPK model predictions are highly sensitive to urinary clearance rate, such that changes in it significantly impact predicted RAIU inhibition for a particular life stage and perchlorate dose. For each of the 17 distinct populations or life stages evaluated in the model, EPA used one of two different urinary clearance values: 0.05 L/h-kg for the pregnant woman at gestational weeks 13, 20, and 40 (which also impacts the RAIU prediction for the fetus at gestational week 40), and 0.13 L/h-kg for all other populations/life stages. If one calculates urinary clearance in L/h by multiplying these values by the corresponding scaled body weight, the resulting urinary clearance rates for the pregnant woman are much lower than for all other adults evaluated by the model: urinary clearance rates range from 1.20 to 1.32 L/h for the pregnant woman, 3.21 to 3.28 L/h for the lactating woman, 3.08 L/h for the woman of child-bearing age, and 3.15 L/hr for the average adult. The assumption of reduced urinary excretion during pregnancy, however, is not supported by the bulk of the scientific literature. The perchlorate urinary clearance rates used in the model are based on data collected in Greer et al. (2002). These values were originally described in the Merrill et al. (2005) model for adult humans, and were incorporated into the Clewell et al. (2003a, 2003b, 2007) models. Per Merrill et al. (2005), the 0.13 L/h-kg clearance rate is based on the mean "fit" urinary clearance rate for perchlorate for adult males and females (nonpregnant) in the Greer et al. (2002) study; the values for the 23 individuals in that study ranged from 0.06 to 0.24 L/h-kg. According to Clewell et al. (2007), the 0.05 L/h-kg urinary clearance value applied to the pregnant woman (and fetus) was selected from the lower bound of this range, in part because this lower value was consistent with data from a study of perchlorate-exposed pregnant women in Chile (Tellez et al., 2005). Clewell et al. (2007) describes their rationale as follows: In the nonpregnant adult model, Merrill and coauthors (2005a) fitted the perchlorate urinary clearance value to each individual for which data were available and noted a marked variation between subjects. Values for urinary clearance (ClUcp) ranged from 0.05 to 0.24 ng/L-h [sic], with an average of 0.13 ng/L-h [sic]. Using the lower bound of these values (0.05 ng/L) [sic], the gestation model predicted serum levels were within the range of the experimental values of Tellez et al. (2005)... Since the lower clearance value lies within the range of the normal adult, improves the perchlorate prediction, and yields a more conservative estimate of risk, it was

used for all subsequent maternal simulations and dose metric calculations. Note that the actual lower bound of the perchlorate urinary clearance range from Greer et al. (2002) (reported in Merrill et al. (2005)) is 0.06 L/h-kg, not 0.05 L/h-kg. Further, this value of 0.06 L/h-kg is for an adult male; no pregnant women were included in the study population, and the lowest reported value for any woman is 0.09 L/h-kg. Clewell et al. (2007) indicated the lower-bound value from Greer et al. (2002) is consistent with data collected by Tellez et al. (2005). Tellez et al. (2005) evaluated perchlorate exposure in pregnant women in three cities in Chile exposed to perchlorate in water at average concentrations ranging from 0.5 to 114 ug/L. This paper says that urinary perchlorate was measured during two prenatal visits and one postnatal visit, and reported excretion in units of ug/L and ug/g creatinine. Unfortunately, no data are provided in the paper on time course of excretion, so it is unclear how Clewell et al. (2007) established that the lower bound of the urinary clearance rate for these populations was 0.05 L/h-kg. In selecting a urinary clearance value to use for the pregnant woman, EPA considered two additional values: clearance during pregnancy in the average adult based on Aboul-Khair et al. (1964); and clearance during pregnancy equal to nonpregnant average values. Aboul-Khair et al. (1964) evaluated urinary clearance of iodide in pregnant women in the United States and reported that "renal (urinary) clearance for iodide is elevated to as much as two times control (nonpregnant) values during pregnancy, and, while clearance then declines fairly rapidly towards control after birth, it is still elevated in the first couple of months" (U.S. EPA, 2009a). EPA assumed that urinary clearance of perchlorate would have the same pregnant to nonpregnant ratio reported by Aboul- Khair et al. (1964). EPA ran the model using all three values. Of these values, the clearance value used by Clewell et al. (2007) resulted in the highest predicted RAIU inhibition. For example, at a dose of 7 ug/kg-d (a dose ten times the RfD of 0.7 mg/kg-d), EPA (2009a) reports a RAIU inhibition for the fetus of 11% using the Clewell et al. (2007) clearance value, 5.2% using the average non- pregnant adult clearance value, and 3.4% using the Aboul-Khair et al. (1964) clearance value. Regarding final selection of this value, EPA (2009a) says: Since there are no conclusive human pregnancy data to distinguish which of these alternatives is more likely, EPA selected option 1, the lower clearance value reported in the peer-reviewed paper by Clewell et al. (2007) for relative response estimation (life stage sensitivity analysis), since this value leads to the most sensitive predictions... While this analysis uses the lowest urinary clearance value among the alternatives evaluated, it does not provide an overall upper-bound effect estimate because the impact of uncertainty and variability in parameters other than those examined here (e.g., uncertainty in thyroid NIS parameters and interindividual variability in urinary excretion) was not evaluated. Thus, EPA selected a urinary clearance value for this population based on a nonscience consideration that lacked corroborating data in the face of other data supporting a higher value. EPA states that selection of this value is not meant to reflect uncertainty or a bounded estimate. This is inconsistent with the statement in the Notice regarding the use of conservatism in the model (U.S. EPA, 2009a), that: The PBPK model for each life stage is presumed to represent a typical or average individual from that life stage. Thus, in evaluating specific PBPK parameter choices, especially for urinary clearance, EPA's objective was to ensure that the values appropriately represented an average or central value for a given life stage and age. EPA further elaborates (U.S. EPA, 2009a): In the case where more than one alternative clearance value appeared to be equally likely (i.e., had a similar quality and amount of supporting data), then the more "sensitive" option was selected (i.e., the option that leads to predictions of the highest sensitivity to perchlorate- induced RAIU). The overall analysis did not seek to select parameters associated with highest predicted effect and is not intended to represent an upper-bound estimate of the average effect of perchlorate in these populations. Modeling choices are assumed to represent the best or most likely (central) estimate for an average individual within the population. There is uncertainty about the average, and EPA has selected from within the range of uncertainty, but there is still expected to be population variability around the

model predictions based on that choice, with the model prediction being near the center of the distribution. The Notice states that the urinary clearance value was selected to "represent the best or most likely (central) estimate for an average individual within the population." Selecting the lowest urinary excretion value-one that produces the highest estimate of RAIU inhibition-is not the "average." The Notice declares that all three clearance values considered had a similar quality and amount of supporting data; in fact, this cannot be true based on the information presented. The 0.05 L/h-kg value was of low scientific quality (it is not supported by either source EPA cites as its primary basis, i.e., Greer et al. (2002) or Tellez et al. (2005)) and higher values are better supported by the scientific literature, as discussed below. The scientific literature shows that, although minimal, data are available on perchlorate urinary clearance or excretion rates during pregnancy, but do not suggest lower excretion of perchlorate during pregnancy. In the study of Chilean women, Tellez et al. (2005) reported higher urinary perchlorate excretion (measured as ug/g creatinine) during pregnancy relative to postpartum for women in two of the three cities evaluated (Chanaral and Taltal, which had mean concentrations of perchlorate in tap water of 5.8 and 114 ug/L). In the "low perchlorate" city (Antofagasta, with a mean tap water concentration of 0.5 ug/L), excretion was somewhat higher postpartum. Based on urine samples collected during the NHANES 2001-2002 study, Blount et al. (2007) reported higher urinary perchlorate in pregnant women (mean 3.27 ug/g creatinine, n = 115), relative to all women of reproductive age (mean 2.97 ug/g creatinine, n = 662). Interpretation of data on urinary clearance or excretion of iodide is complicated by the iodide status of populations; however, Smyth et al. (1997) reported that in an area of moderate iodine intake (median urinary iodide 82 ug/g creatinine), urinary iodide excretion was increased during all three trimesters of pregnancy relative to nonpregnant controls. EPA's selection of the lowest identified urinary clearance value for the pregnant woman and fetus is inconsistent with the statement in the Notice about the Agency's use of conservatism in the model (U.S. EPA, 2009a): The PBPK model for each life stage is presumed to represent a typical or average individual from that life stage. Thus, in evaluating specific PBPK parameter choices, especially for urinary clearance, EPA's objective was to ensure that the values appropriately represented an average or central value for a given life stage and age. EPA further states, "there is still expected to be population variability around the model predictions based on that choice, with the model prediction being near the center of the distribution," and: While this analysis uses the lowest urinary clearance value among the alternatives evaluated, it does not provide an overall upper-bound effect estimate because the impact of uncertainty and variability in parameters other than those examined here (e.g., uncertainty in thyroid NIS parameters and interindividual variability in urinary excretion) was not evaluated. Nonetheless, in practice, selection of the lowest urinary clearance value for two of the subpopulations renders the RAIU inhibition predictions for these populations more conservative than for other populations, making application of model results to risk assessment difficult to interpret from a purely scientific basis.]

In addition to using the best science to support PBPK values, other parameters could be added, such as up-regulation of the NIS. Up-regulation of the NIS represents an adaptive response to iodine deficiency in the thyroid, but EPA (2009b) did not incorporate a mechanism of up-regulation in the EPA model. Incorporation of NIS regulation into the model would more accurately reflect the probable response to perchlorate exposure in the environment.[FN10: Over the past decade, research regarding thyroid autoregulation and the regulation of expression of the NIS has proliferated. Evidence suggests that the NIS is up- regulated in response to iodine deficiency in the thyroid. Up-regulation of the NIS causes the number of NIS membrane proteins to increase; thus, when an individual is iodine deficient, the body increases the number of NIS "pumps" such that the thyroid is more effective at capturing iodide. This is a common adaptive mechanism that many

tissues, including the thyroid gland, use to maintain hormone homeostasis. The Draft EPA Office of the Inspector General (OIG) report (U.S. EPA 2008b) appears to consider up-regulation of NIS expression as well. Earlier versions of the model using the rat did consider up- regulation, and showed no RAIU inhibition in the rat thyroid after 18 days of exposure at perchlorate doses up to 10 mg/kg-d (350,000 ppb assuming default body weight and water intake) (Clewell et al., 2003a). Up-regulation was not included in the human model, "based on the fact that upregulation was not seen in the nonpregnant adult after 2 wk of doses as high as 1 mg ClO4- (Merrill et al., 2005)" and although "the current simulations cover lifetime exposures rather than a few weeks, the accompanying data on thyroid hormones (TSH, T4) still do not show evidence of thyroidal up-regulation (Crump et al., 2000; Tellez et al., 2005)" (Clewell et al., 2007). The NRC report, however, acknowledges the up- regulation of NIS expression, but did not incorporate it into their risk assessment. NRC (2005) states: ...rats compensated for the inhibition within 5 days of perchlorate administration, most likely by increasing the expression of NIS in the thyroid. The data suggest that compensation occurs more quickly in rats because rats have a smaller reserve capacity of thyroid hormones than humans.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28883
EPA Comment Code: 2400

Comment: Parameters used in the PBPK model were selected from inconsistent points within their distributions. For example, as described above, EPA (2009a) selected a lower bound value to describe the urinary clearance of perchlorate for the pregnant woman and fetus. In contrast, EPA reports that the urinary clearance values it selected for all other population subgroups fall in the middle of the range of possible values (U.S. EPA, 2009a). As a result, it is difficult to interpret the model output because it is unclear whether the output represents lower-, middle-, or upper- bound predictions of possible IUI caused by perchlorate exposure."[FN11: When conducting calculations to reflect exposure within a population, each parameter can have a range of possible values. In order for PBPK model output to be meaningful, the basis for selection of specific values within the range of possible values should be described and the relationship to the overall distribution for that parameter should be characterized (e.g., lower-bound, average, median, upper-bound). Further, in the absence of probabilistic assessment, if point estimates are selected for incorporation in the model, a consistent rationale should be applied in choosing values for the various parameters so that the location of the output within the overall distribution can be approximated. For example, when conducting baseline human health risk assessments for a reasonable maximum exposure (RME) scenario, EPA recommends estimating "a conservative exposure case (i.e., well above the average case) that is still within the range of possible exposures," and intake variable values for a given pathway should be selected so that the combination of all intake variables results in an estimate of the reasonable maximum exposure for that pathway (U.S. EPA, 1998a). The objective of evaluating conservative exposures is to generate an upper-bound estimate of exposure below which adverse health effects are unlikely. Note that although EPA presents the impact of alternative urinary clearance assumptions on model-predicted RAIU inhibition in its discussion document on the PBPK model (Table 4-2, U.S. EPA, 2009a), it does not present this information in the Notice.]

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28902
EPA Comment Code: 2400

Comment: IV. CONCLUSIONS

1. The use of scientifically derived PBPK models represents the best scientific approach for evaluating the relative sensitivity of different life stages and to compare to occurrence data. As constructed, however, the perchlorate PBPK model likely overestimates IUI from perchlorate exposures for various life stages. Only when the best available science is shared in a transparent process can the public be empowered to assist the Agency in achieving the best public health decisions. Nonetheless, the predicted levels of IUI in the Notice are very low and would be indistinguishable from fluctuations resulting from differences in diet and feeding styles. No adverse health concern at any life stage would be expected based on exposure to perchlorate at the POD dose (7 ug/kg-d).

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Department of Environmental Protection (NJDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0527
EPA Comment ID: 28909
EPA Comment Code: 2400

Comment: Specific issues on which USEPA requests comments in its August 18, 2009 notice are discussed below:

Interpretation and Application of Physiologically-based Pharmacokinetic (PBPK) Modeling

In the October 10, 2008 notice, the PBPK model was used to evaluate the effects of the proposed HRL, 15 ug/L, on the perchlorate dose reaching the thyroid and to estimate effects on the inhibition of thyroidal iodine uptake in sensitive subpopulations. It was assumed that the fetus of the pregnant woman was the most susceptible subpopulation, and our primary concern was that the exposure and health risks of bottle fed and breast fed infants and older children, as predicted by the PBPK model, were ignored.

Using 90th percentile water intakes, the PBPK model predicts that when water with 15 ug/L perchlorate is used to prepare formula, 7-day and 60-day old bottle-fed infants are exposed to more than 5 times the RfD, and that iodide uptake in 7-day old infants is decreased by 2.2% (Table 4-5). Exposures of 7-day and 60- day breast-fed infants and children 6-12 months and 1-2 years are also predicted to exceed the Reference Dose. Even if the model was to use the median rather than the

90th percentile water intake, the RfD would be greatly exceeded for bottle-fed infants. We recommend that USEPA consider the PBPK model's predictions of exposures and effects in these sensitive infants and children, as well as the exposure of the fetus through the pregnant mother, in evaluating the potential for perchlorate in drinking water to inhibit thyroidal iodine uptake.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination. See response to comment code 5220 for a discussion of

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Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Department of Environmental Protection (NJDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0527
EPA Comment ID: 28910
EPA Comment Code: 2400

Comment: However, there are several concerns that indicate the need for caution in using the PBPK model to determine a health-protective drinking water concentration for perchlorate. First, it is based on average weight babies and average weight healthy adults, including pregnant women. Furthermore, due to lack of availability of the needed data, only 40-week fetuses were considered and it was not possible to model effects on fetuses at earlier stages of development. Thus, the PBPK model may not adequately predict the effects of perchlorate on those who are particularly susceptible to its effects, such as low birth weight infants, mothers or infants with iodine deficiency or hypothyroidism, and fetuses younger than 40 weeks.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Danielle Blacet
Commenter Organization: Association of California Water Agencies
EPA Document ID: EPA-HQ-OW-2009-0297-0208
EPA Comment ID: 28923
EPA Comment Code: 2400

Comment: Response to questions posed by USEPA:

1) PBPK Modeling (page 41886)

ACWA does not take issue with this type of pharmacokinetic modeling. However, in previous regulatory determinations and drinking water standards, pharmacokinetic models were only used in a secondary fashion, if at all, after the toxic end point was identified by the relevant epidemiological data. We would like clarification on the justification for modifying existing procedures.

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group (EWG)
EPA Document ID: EPA-HQ-OW-2009-0297-0499
EPA Comment ID: 28930

EPA Comment Code: 2400

Comment: In this notice, the Agency specifically requests comments on certain approaches within their assessment, including the following:

1) Use of PBPK modeling analysis to inform the regulatory determination for perchlorate

2) Appropriateness of alternative health reference levels (HRLs) described in the notice to address and account for risk to all potentially sensitive life stages

3) Occurrence analysis including use of Bayesian model and U.S. Census data

Use of PBPK model: EWG supports the use of the PBPK model to estimate the extent of iodine uptake inhibition in sensitive life stages only if significant limitations of the current model are addressed.

In this notice, one of the approaches that the Agency considers is the following: "... use the PBPK modeling analysis to explore the relative sensitivity of the various life stages of concern to a fixed dose such as the point of departure (POD) or the reference dose (RfD)." In this case, the agency notes that the "POD is the lowest dose administered in the Greer et al clinical study...".

The Greer study included only 37 study participants who were divided into several study groups and administered different doses of perchlorate for 14 days (Greer et al 2002). The researchers determined that a daily perchlorate dose of 0.007 mg/kg/day was the no observed effect level (NOEL); the results from this study were used by the National Academy of Sciences (NAS) in setting the reference dose (RfD) for perchlorate of 0.7 ug/kg/day.

The Greer study results and assumptions drawn from them have been questioned in a peer-reviewed article that was published in Environmental Health Perspectives in 2005 (Ginsberg and Rice 2005). Two toxicologists, one from the Connecticut Department of Public Health and the other from the Maine Bureau of Health, conducted an analysis of the raw data from the Greer study and concluded the following: "Individual results of Greer et al. point to an effect in four of the seven individuals tested at the lowest dose (0.007 mg/kg/day), indicating that this dose is an effect level." In other words, while Greer et al. and the NAS both concluded that 0.007 mg/kg/day is a no observed effect level (NOEL), closer analysis of the data reveals that four of the seven study subjects in this group experienced effects at this dose, thereby invalidating 0.007 mg/kg/day as a NOEL.

The Massachusetts Department of Environmental Protection (Mass DEP), which has set the most stringent drinking water standard for perchlorate nationally, had the following observations about the Greer study:

"MassDEP has concerns about the lowest dose in the Greer study being a no-effect level based on the facts that: due to the small number of subjects in the lowest dose group, there is low power to detect a statistically significant effect; averaging of group responses obscures positive individual inhibition; a non- statistically significant IUI (iodine uptake inhibition) effect was observed at the lowest dose tested; and, good low dose corroborating data is lacking" (MassDEP 2006).

In light of these valid criticisms of the Greer study, it is clear that any exposure modeling based on the results of this study, including the agency's current proposal to use PBPK modeling with a POD derived from this particular study, would not be accurate. The PBPK model also does not address iodine status, an important factor in determining vulnerability to perchlorate (Blount et al 2006b).

Response: See response to comment code 2100 for a discussion of the Reference Dose for perchlorate. See response to comment code 2300 for a discussion of EPA's use of the PBPK models.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 29101
EPA Comment Code: 2400

Comment: EPA failed to provide any data to support its conclusion, and is contradicted by the results of PBPK modeling as reported by staff experts and in the Federal Register notice.[FN53: EPA Office of Research and Development. Inhibition of the sodium-iodide symporter by perchlorate: An evaluation of lifestage sensitivity using physiologically-based pharmacokinetic (PBPK) modeling. Preliminary Draft. October 2, 2008. EPA/600/R-08/106A. Docket ID No. EPA-HQ-OW-2008-0692-0076.]

Response: See response to comment code 2300 for a discussion of PBPK modeling in this regulatory determination.

EPA Comment Code: 2410 Use of PBPK model to select life-stage-specific HRLs

Individual Comments

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0653
EPA Comment ID: 28558
EPA Comment Code: 2410

Comment: The Agency showed additional conservatism from the NRC recommendation in adjusting the preliminary guidance for perchlorate to 15 ppb in water in order to account for the relative source contributions of drinking water and dietary sources in order to protect pregnant women and their fetuses. This level, as demonstrated by the physiologically-based pharmokinetic (PBPK) modeling, is likewise protective of other potentially sensitive lifestages. The PBPK modeling for infants and young children do not exceed the 10x (i.e. ten fold) intraspecies factor set from the adult values thereby showing that the 10x intraspecies factor is protective and provides no justification for increasing an uncertainty factor for perchlorate beyond the default (i.e. ten fold or 10x). For this reason, EPA has no basis for adjusting the reference dose (RfD) of 0.0007 mg/kg/day, or the methodology for setting the HAL based on a 70 kg adult consuming two (2) liters of water. This traditional method, used previously by EPA with SDWA contaminants is sufficiently conservative as the level of water consumed (two liters) is the 99th percentile estimate, and, this RfD is based on a no-effect level (NOEL) from the Greer et. al. 2002 study rather than a no adverse effect level (NOAEL).

Response: EPA does not agree that allowance for contributions of perchlorate from sources other than drinking water introduces additional conservatism. Rather, allowance for other sources of perchlorate permits EPA to establish a concentration of perchlorate in drinking water that maintains a tolerable risk level without adjusting the existing background.

The modeled estimates of exposure to various life stages, presented as alternative HRLs in the August 2009 supplemental request for comments, indicate values as much as seven times that for pregnant females. However, the life stage variability in the model estimates reflects pharmacokinetics only. Pharmacodynamic variability is not reflected nor can it be estimated using the modified Clewell (2007) model. Data permitting estimation of pharmodynamic variability among life stages is not available. Therefore, it is not possible to determine whether the alternative HRLs are within the variability reflected in the RfD. EPA will continue to evaluate the significance of varying exposure estimates as the Agency develops a NPDWR for perchlorate.

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 28750
EPA Comment Code: 2410

Comment: b. EPA requests comment on the utility of the PBPK model for predicting the impact of different perchlorate drinking water concentrations on sensitive life stages to inform HRL selection.

Comment A.4.b.1: Additional refinement and supporting rationale for the current configuration of the PBPK model is needed based on actual human study observations to enable EPA to use this model for the stated purpose. This refinement should include an evaluation of the potential for sustained FT3 and/or FT4 reductions in humans including pregnant women, fetuses, and neonates. Human data (likely including reproductive age females and adolescents) on the pharmacokinetic use of perchlorate for lowering thyroxine levels in hyperthyroid patients are available in both published reports and likely also in clinical trials and unpublished data from various research groups. A critical step to support use of the PBPK model should include development of a quantitative term that defines the relationship between steady state blood perchlorate and the decrement in free and total thyroid hormones in reproductive age females. Much of the data needed for this refinement and supporting rationale are not currently available. Consequently, the EPA should send out queries searching for available unpublished human datasets relevant to the modeling evaluation, and encourage the development of appropriate studies to acquire these data and permit support for and use of the PBPK model.

One example of technical difficulties in the model is the consideration of iodine deficiency and associated NIS upregulation in the pregnant mother, fetus, and neonate. Additional clinical data are needed for adults (including pregnant women, and in neonates) concerning thyroidal iodine capacity and the impact of NIS upregulation on thyroidal iodine uptake and/or thyroxine levels. Also, additional studies of other adults are needed to evaluate the effects of temporary iodine deficiency and NIS upregulation on perchlorate competitive inhibition of thyroidal iodine uptake and/or free thyroid hormone levels. This additional research would provide useful data to consider in further refining the PBPK model to accurately reflect the effects of iodine deficiency in pregnant women, fetuses and neonates.

Response: See response to comment ID 28800 under comment code 2410.
EPA agrees that the PBPK model used in preparation of the 2008 Preliminary Regulatory Determination requires further refinement before it can be used to develop an HRL. EPA also agrees that the data required to permit the necessary modifications does not exist at this time. As additional data become available, EPA will be able to determine whether further effort to develop a PBPK model for different life stages exposed to perchlorate is warranted. The attributes and components of that model cannot be determined at this time.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28800
EPA Comment Code: 2410

Comment: b. Utility of the PBPK model for predicting the impact of different perchlorate drinking water concentrations on sensitive life stages to inform the HRL

NRDC Response: The PBPK model can predict the impacts of perchlorate water contamination on different life stages; it predicts that sensitive populations are not protected by the proposed HRL

As detailed in our response above, the EPA staff report issued on October 2, 2008, describes findings from the PBPK model that consuming water that was contaminated at the HRL of 15 ug/L would lead to bottle-fed infants exceeding the reference dose by 5- fold and young children exceeding the reference dose by 2.8-fold, based on average food contamination rates, average body weights, and 90th percentile water consumption rates for each age group.[FN33: EPA Office of Research and Development. Inhibition of the sodium-iodide symporter by perchlorate: An evaluation of lifestage sensitivity using physiologically-based pharmacokinetic (PBPK) modeling. Preliminary Draft. October 2, 2008. Table 4. EPA/600/R-08/106A. Docket ID No. EPA-HQ-OW-2008- 0692-0076.]

These findings from the PBPK model analysis are supported by other published studies. A related study estimated perchlorate doses that correspond to urinary perchlorate excretion (hereinafter referred to as "Blount (2007)").[FN34: Blount BC, Valentin-Blasini L, Osterloh JD, Mauldin JP, Pirkle JL. Perchlorate exposure of the US Population, 2001-2002. J Expo Sci Environ Epidemiol. 2007 Jul;17(4):400-7. Epub 2006 Oct 18.] Calculating doses based on urinary excretion is feasible because perchlorate is not metabolized and has a short half- life of approximately 8 hours.[FN35: Ibid.] Blount (2007) showed that the adjusted geometric mean for perchlorate exposure in women was 0.059 ug/kg-day, and the 95th percentile exposure was 0.215 ug/kg-day. This means that the adverse effects of decreased serum T4 and increased TSH in women with low dietary iodide (that is, urinary iodide below 100 ug/L) described by Blount (2006) are occurring at perchlorate exposures below the RfD of 0.7 ug/kg- day.[FN36: Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environ Health Perspect. 2006 Dec;114(12):1865-71.] As such, the proposed HRL of 15 ppb will not protect sensitive subpopulations.

An extensive literature review and health assessment by Ginsburg et al.[FN37: GL Ginsburg, DB Hattis, RT Zoeller, and DC Rice. 2007. Evaluation of the U.S. EPA/OSWER preliminary remediation goal for perchlorate in groundwater: Focus on exposure to nursing infants. Environ Health Perspect. 115(3):361-369. http://www.ehponline.org/members/2006/9533/9533.html] published since the NRC review found that "drinking-water perchlorate must be < 6.9 ug/L to keep the median, and < 1.3 ug/L to keep the 90th-percentile nursing infant exposure below the RfD."[FN38: GL Ginsburg, DB Hattis, RT Zoeller, and DC Rice. 2007. Evaluation of the U.S. EPA/OSWER preliminary remediation goal for perchlorate in groundwater: Focus on exposure to nursing infants. Environ Health Perspect. 115(3):361-369.] Based on both exposure and toxicity information, and data on sensitive populations, the proposed HRL of 15 ppb, which is more than twice as high as the limit proposed by Ginsberg et al, will leave significant portions of the population at risk.

Response: EPA agrees that reassessing exposure assumptions and other life stages warrants further consideration.
EPA also considered applying the model directly to the exposures of other sensitive life stages to develop HRLs for these life stages. The NRC (2005) identified "the fetuses of pregnant women who might have hypothyroidism or iodide deficiency" as "the most sensitive population," but also identified infants and developing children as additional "sensitive populations." EPA derived potential alternative HRLs for 14 different life stages as presented in the supplemental request for comments (EPA 2009). Alternative HRLs are estimates of the maximum concentration of perchlorate that can be consumed in drinking water without an individual's total perchlorate dose

from food and water exceeding the RfD. EPA agrees that exposures reported in the literature suggest some life stages may be exposed to quantities of perchlorate above the RfD.

National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276pp.

EPA Comment Code: 2420 Suggestions for alternative ways to use the PBPK model to inform the regulatory determination

Individual Comments

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 28751
EPA Comment Code: 2420

Comment: c. EPA requests suggestions for ways to use the PBPK modeling analysis to inform the regulatory determination for perchlorate that are different from those described in this notice or the October 10, 2008 notice.

Comment A.4.c.1: Prior to use of the PBPK model as a part of the regulatory determination, the range and primary sources of uncertainty in the model output should be evaluated and described. Once properly validated and supported, the model may be used to evaluate a number of physiological and pharmacokinetic impacts of perchlorate competitive inhibition, including alternative approaches of basing the reference dose on clinically important changes in thyroidal iodine uptake and/or thyroxine levels.

Response: The modified Clewell (2007) model was subjected to peer review by the Office of Research and Development, EPA. However, EPA agrees that additional modification and refinement of the model is needed before it can be used to develop an HRL to determine the need to establish an NPDWR. The extent and nature of modifications and refinements needed are not clear at this time.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28801
EPA Comment Code: 2420

Comment: c. Using the PBPK modeling analysis to inform the regulatory determination for perchlorate that is different from those described in the October, 2008 FR notice

NRDC response: The PBPK model may be used to derive a science-based adjustment factor; the model support an adjustment factor of at least 15-fold to inform the regulatory determination for perchlorate.

EPA normally uses a 10-fold default uncertainty factor to adjust for variations among individuals, called the intraspecies factor, when the Agency lacks adequate data to calculate variability between individuals. EPA used this 10- fold intraspecies factor for its perchlorate hazard assessment on its IRIS database: "An intraspecies uncertainty factor of 10 is applied to protect the most sensitive population, the fetuses of pregnant women who might have hypothyroidism or iodide

deficiency."[FN39: EPA. IRIS database. Perchlorate and perchlorate salts. http://www.epa.gov/ncea/iris/subst/1007.htm#revhis] The Agency has adopted the practice of describing the default 10-fold intraspecies factor as being comprised of the product of two 3-fold factors, one for harmacokinetic variability, and the other for pharmacodynamic variability.[FN40: US EPA. Office of the Science Advisor: Staff Paper, Risk Assessment Principles & Practices. Page 69, Section 4.3.2. EPA/100-B-04/001. March, 2004. http://www.epa.gov/osa/pdfs/ratf-final.pdf] Pharmacokinetics describes the way that a compound such as perchlorate moves through the body, including its absorption, distribution, metabolism and excretion. In contrast, pharmacodynamics describes what the compound does in the body, including depressing, stimulating, irritating, or killing cells or systems.

According to the IRIS glossary of terms, a physiologically based pharmacokinetic (PBPK) model estimates the dose of a compound to a target organ or tissue by calculating the rate of absorption in the body, the distribution among target organs, the metabolism of the compound, and the excretion of the compound.[FN41: IRIS Glossary. Physiologically Based Pharmacokinetic (PBPK) Model. http://www.epa.gov/ncea/iris/help_gloss.htm#p] In other words, the PBPK model, by definition and design, estimates the pharmacokinetics of a compound.

The data from EPA's staff report shows that EPA's reliance on a default uncertainty factor of 10 underestimates the variability between fetuses and adults. The Executive Summary of the staff report states that "at a perchlorate dose of 7 ug/kg-day, the percent RAIU inhibition predicted by the model for the near-term fetus is 5-fold greater than the average adult....The same analysis predicts percent RAIU inhibition approximately 1-2 fold higher for the breast- fed and bottle-fed infant (7-60 days) than for the average adult."[FN42: See EPA Staff Paper, Executive Summary, p. 4 and Table 3; see also 73 Fed. Reg. 60278.] More specifically, for perchlorate, the variability between a near-term fetus (40 weeks gestation) and an adult is 5.3-fold. Therefore, the PBPK model supports a pharmacokinetic adjustment factor of at least 5-fold.

The Agency has no information from the PBPK model, or from other data, to develop an intraspecies uncertainty factor for pharmacodynamic variability, particularly between adults and sensitive lifestages. Therefore, EPA should retain a factor of at least 3-fold or more to adjust for pharmacodynamic uncertainty, consistent with its current practice.

To be consistent with EPA policy and practice, EPA should use a total intraspecies uncertainty factor of 15-fold, rather than 10 fold. Based on the data from the PBPK model to support a pharmacokinetic intraspecies variability factor of 5, and the lack of pharmacodynamic data to support a default factor of 3, the use of a 15-fold uncertainty factor is supported by the available data.

Response: EPA agrees that the modeled estimates of alternative HRLs reflect only pharmacokinetics and do not consider uncertainty due to pharmacodynamics. EPA's RfDs typically factor in both, with a standard apportionment of 3.16 for each. EPA does not believe that it is possible to determine whether a 10-fold uncertainty factor is sufficient to reflect both pharmacokinetics and pharmacodynamics. However, EPA acknowledges that 10X may be insufficient. Data do not currently exist to provide an estimate of the pharmacodynamic component of the intraspecies uncertainty factor.

Commenter Name:

Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28884
EPA Comment Code: 2420

Comment: 3. EPA requests suggestions for ways to use the PBPK modeling analysis to inform the regulatory determination for perchlorate that are different from those described in this notice or the October 10, 2008 notice.

The PBPK model can provide useful information to characterize the relative sensitivity of this life stage if model parameters are scientifically defensible and selected from comparable points within their parameter distributions, and if nonscientific considerations do not introduce unexplained bias into the selection of parameter values. To be most useful, EPA should use probabilistic methods to characterize the uncertainty and variability around parameter distributions and the range and likelihood associated with model-predicted RAIU inhibition for each population or life stage. Use of probabilistic methods is consistent with the Agency's current recommendations for use of probabilistic methods in risk assessment to help inform risk management decisions.[FN12: http://www.epa.gov/fedrgstr/EPA-RESEARCH/2009/August/Day-18/r19755.htm; http://vvww.epa.gov/raf/prawhitepaper/pdf/pra_mgr_summary_0609.pdf.]

Additional considerations would provide perspective on the significance of the IUI associated with low dose perchlorate exposure. For example, EPA should present the change in RAIU inhibition when the RfD is modeled rather than the Greer et al. (2002) POD, which is ten fold higher.

Response: EPA believes that the modified Clewell (2007) model is useful in examining which life stages are most susceptible to the effects of perchlorate. For example, the model indicates that a fetus may be seven times more sensitive to the effects of perchlorate than a pregnant woman. The model also allows for the estimation of the concentration of perchlorate in breast milk (thus breast-fed infant exposure) at various maternal perchlorate exposure levels. Data do not exist at this time to permit a more expansive development of the model for various life stages.

EPA believes that the RfD derived by the NRC using the Greer et al. (2002) remains the appropriate estimate of health effects due to perchlorate for use in assessment of risk.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28885
EPA Comment Code: 2420

Comment: Also, multiple chemical agents affect the uptake of iodide into the thyroid in the same way as perchlorate. These goitrogens, which include thiocyanate and nitrate, can be found naturally in common foods, including produce, milk, and cured meats. Incorporation of thiocyanate and nitrate exposure into the PBPK model should provide useful information on the relative IUI caused by exposure to these agents and to perchlorate. Thus, daily diets for children and adults including these foods are predicted to have a greater effect on IUI than would result from drinking two liters of water containing perchlorate at environmentally relevant levels (e g., estimated perchlorate drinking water equivalent concentrations associated with the thiocyanate and nitrate present in these

diets are estimated to be at least 1,500 to 29,000 ppb). Based on these data, the contribution of perchlorate in drinking water at a concentration of 20 ppb (assuming consumption of 2 liters per day) to total daily IUI associated with a typical diet would be a fraction of these values.

Response: EPA does not disagree that a total iodine inhibitor load, including naturally-occurring NIS inhibitors, should be considered. However, adequate data do not exist at this time to characterize adequately the relative affinity of various iodide uptake inhibitors for the NIS receptor. In addition, no data exist to characterize their relative potency in impacting thyroid hormone levels. Given this lack of data, EPA believes that it is prudent to consider the potential adverse health effects for perchlorate independently until data are developed to permit consideration of multiple goitrogens jointly.

EPA Comment Code: 2500 Other health effects studies, models, and data for EPA to consider (besides NAS/NRC report, NHANES biomonitoring data, and PBPK models already evaluated)

Individual Comments

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0648
EPA Comment ID: 19991
EPA Comment Code: 2500

Comment: According to the office of environmental health hazard assessment, see link: http://www.oehha.ca.gov/public_info/facts/faqperchlorate.html, perchlorate has not been scientfically proven to cause cancer in humans at the doses likely to be in drinking water. The University of California conducted 3 separate studies on the topic.

Response: EPA respectfully disagrees with this comment. In 2003, the National Research Council (NRC) of the National Academy of Sciences (NAS) was asked by EPA to assess the current state of the sciences regarding potential adverse effects of perchlorate exposure and to determine whether EPA's prior perchlorate risk assessment findings were consistent with current scientific evidence. In a NRC 2005 review ("Health Implications of Perchlorate Ingestion", (NRC, 2005)), the NRC recommended that data from the Greer et al. (2002) human clinical study be used as the basis for deriving a perchlorate reference dose (RfD) (NRC, 2005). From this Greer et al. (2002) human clinical study, the statistical no observed effect level (NOEL) for the perchlorate-induced inhibition of thyroid iodide uptake was determined to be 7.0 ug/kg, which corresponded to an iodide uptake inhibition of 1.8 %. The NRC concluded that the most health protective and scientifically valid approach to deriving a reference dose for perchlorate was to base the perchlorate RfD on the inhibition of iodide uptake by the thyroid, and that iodide uptake inhibition, though not an adverse effect per se, is the most appropriate precursor event, and would precede any more severe adverse health effects of perchlorate exposure in humans. The NRC recommended basing the RfD on a precursor to an adverse effect rather than an adverse effect, per se. The precursor event precedes a downstream adverse effect in the dose response continuum. In this case, NRC used prevention of iodide uptake inhibition, a precursor to adverse thyroid effects, to establish a level at which no adverse effects would be anticipated in exposed populations. This approach is consistent with the Agency's policy on the use of precursor events when appropriate in establishing the critical effect upon which an RfD is based (U.S. EPA, 2002). The NRC recommended that EPA apply an uncertainty factor of 10 to this NOEL of 7.0 ug/kg for the perchlorate-induced inhibition of thyroid iodide uptake, to account for differences in sensitivity between healthy adults and the most sensitive sub-population, consisting of fetuses of pregnant women who might have hypothyroidism or iodide deficiency. Iodide uptake inhibition has been identified in the literature as an area of concern in connection with increasing the risk of neurodevelopmental impairment in fetuses of high-risk mothers. The NRC viewed the recommended uncertainty factor of 10 as conservative and protective of health, given that the NOEL is based on a non-adverse effect (iodide uptake inhibition) which precedes the adverse effect in a continuum of possible adverse biological effects of perchlorate exposure. NRC recommended that using a non-adverse effect that is upstream of the adverse effect

represents a more conservative, health-protective approach to the risk assessment for perchlorate, noting that the purpose of the 10-fold uncertainty factor is to protect sensitive subpopulations in the face of uncertainty regarding their relative sensitivity to perchlorate exposure. EPA has adopted the NRC's recommendations in its "Integrated Risk Information System" (IRIS) (USEPA 2005), resulting in an RfD of 0.7 ug/kg/day, which was derived by applying a 10-fold (10x) uncertainty factor to the NOEL of 7.0 ug/kg/day. Greer MA, Goodman G, Pleus RC, Greer SE. Environ Health Perspect. 2002 Sep;110(9):927-37. Erratum in: Environ Health Perspect. 2005 Nov;113(11):A732. National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276pp. USEPA. 2002. A review of the reference dose and reference concentration processes. Risk Assessment Forum, Washington, DC; EPA/630/P–02/0002F. USEPA. 2005. "Integrated Risk Information System (IRIS), Perchlorate and Perchlorate Salts." February 2005.

Commenter Name: Tatjana and Jeremy Thomas
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0669
EPA Comment ID: 20242
EPA Comment Code: 2500

Comment: >From New York Times 3/2/04 ...".The study found crude effects on rats' brains from exposure to perchlorate. Parts of the brains were enlarged. ....In the same study, benign tumors were spotted on two 19-week-old baby rats out of a group of 30 whose mothers had been exposed to high levels of perchlorate. Scientists from the environmental agency say it is unusual to see tumors in baby rats that young, leading them to believe that something must have occurred in the womb."

Concerned Citizen and a pregnant mother of two.

Attachments

EPA-HQ-OW-2008-0692-0669.1 Comment attachment submitted by T. Thomas

EPA-HQ-OW-2008-0692-0669.2 Comment attachment submitted by T. Thomas

Jeremy and Tatjana Thomas 40268 205th Avenue Pittsfield, IL 62363 (217) 285-5951

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of

health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Crystal D. Lay
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1557
EPA Comment ID: 20523
EPA Comment Code: 2500

Comment: 1. Perchlorate interferes with the functioning of the thyroid gland which can disrupt metabolism regulation in adults. However, the effects on children can be much worse causing irreversible developmental problems. This is particularly concerning when the U.S. Food and Drug Administration's Total Diet Study:

Dietary Intake of Perchlorate and Iodine study revealed that children two years of age have the highest total perchlorate intake per day and infants have the second highest perchlorate intake per day. 2. The RFD of .07 Âµg/kg translates to a drinking water equivalent of 24.5 ppb, based on 2 liters consumed by an adult daily. However, this assumes that the only source of perchlorate is drinking water. The 2004-2005 Exploratory Survey Data on Perchlorate in Food Samples listed several foods that were found to have perchlorate. One milk sample revealed levels of over 10 ppb Âµg/L. Samples of green beans revealed levels as high as 25.9 ppb. Samples of oranges revealed levels as high as 23.3 ppb. This is alarming as these foods are all essential to growing children who may be more prone to higher levels of perchlorate already. The translated RFD of 0.7 Âµg/kg to 24.5 ppb is calculated for adults. This level may be even lower for children and does not include any

perchlorate intake from food they may consume. Another serious consideration is the seemingly high levels of perchlorate that could be consumed by infants if fed formula mixed with drinking water. For the reasons stated above, I urge EPA to reconsider setting a national maximum contaminant level for perchlorate in drinking water. The states that have already imposed a maximum contaminant level for perchlorate have set the standard much lower than 24.5 ppb, suggesting that those states have concluded that a safe level of perchlorate intake is less than 24.5 ppb.

Respectfully submitted,

Crystal D. Lay

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of

health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Jimmy Spearow
Commenter Organization: Sacramento Chapter, Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-1672
EPA Comment ID: 20589
EPA Comment Code: 2500

Comment: Dear EPA This is a Public Comment Regarding EPA's refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692).

Perchlorate is a chemical in rocket fuel that has been associated with decreased thyroid hormone levels in pregnant women, newborns and young children. Thyroid hormone is critical for growth and development, especially in the brains of fetuses and children. Perchlorate inhibits iodine uptake and the synthesis of thyroid hormone by the thyroid gland. The CDC showed that exposure to perchlorate levels as low as 5 ppb was associated with decreased thyroid hormone levels, especially in women with lower iodine levels. In other words, exposures at levels significantly lower than the level EPA assumes is "safe" i.e., the EPA RfD of 24.5 ppb, were linked to a lowering of thyroid hormone levels that can cause significant adverse health effects in exposed women and fetuses. Since over 16 million Americans are at risk of exposure to elevated levels of perchlorate, extrapolation of this study to the entire US population indicates that approximately 2 million women of childbearing age are at risk from abnormally low thyroid hormone levels.

Adequate levels of thyroid hormone are also critical to normal growth and cognitive development in infants. Infants are likely to be particularly vulnerable to perchlorate since they have rapid turnover of thyroid hormone, as well as, low reserves of thyroid hormone.

Response: EPA acknowledges and thanks you for providing comments. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Carol Bigelow
Commenter Organization: University of Massachusetts
EPA Document ID: EPA-HQ-OW-2008-0692-1427
EPA Comment ID: 20626
EPA Comment Code: 2500

Comment: NOVEMBER 10 2008

US Environmental Protection Agency Office of Water Docket (Mailcode: 2822T) 1200 Pennsylvania Avenue, NW Washington, DC 20460

RE: Comments on Regulatory Determination on Perchlorate Docket EPA-HQ- OW-2008-0692

Drs. Carol Bigelow, Larry Schwartz, and R. Thomas Zoeller are pleased to submit comments to the US EPA on Docket ID No. EPA-HQ-OW-2008-0692, entitled "Drinking Water: Preliminary Regulatory Determination on Perchlorate". In brief, the authors of docket ID No. EPA-HQ-OW-2008-0692 propose that there be no national primary drinking water regulation, the rationale being that such would not present a "meaningful opportunity for health risk reduction for persons served by public water systems". EPA's proposal not to regulate perchlorate in public water systems:

(1) Lacks the requisite scientific basis. Specifically, EPA regularly cites the nearly 4 year-old NAS report (NRC, 2005) without a critical evaluation of the science underlying the document and how new information should be integrated into it. This issue is most germane in the emphasis on the pregnant woman and fetus as the most sensitive population to perchlorate exposure. EPA fails to consider published, peer-reviewed data demonstrating that the current RfD for perchlorate exposure is not protective of neonates and infants (Ginsberg and Rice, 2005; Ginsberg et al., 2007).

(2) Lacks critical evaluation of the literature employed to justify its decision. Methodologically sound research indicates an association between perchlorate exposure and thyroid function in adult women with low iodine intake (Blount et al., 2006a; Steinmaus et al., 2007). If infants are no more sensitive to perchlorate than adult women, brain damage will occur at the median level of perchlorate exposure, according to published data (reviewed by (Ginsberg et al., 2007)). Thus, the CDC study should reasonably replace the 6 year-old "Greer Study" (Greer et al., 2002) as the point of departure for RfD development.

(3) Fails to critically evaluate the reliability of null findings. EPA justifies ignoring the Blount Study using a series of studies that identify no relationship between perchlorate exposure and thyroid function in humans. However, EPA is apparently unaware of published data describing the variability of serum thyroid hormone measures in adults (Andersen et al., 2002; Andersen et al., 2003) and in neonates (Herbstman et al., 2008a; Herbstman et al., 2008b). It is our opinion that critical analysis of the null findings employed by EPA to justify ignoring the findings in the Blount Study will demonstrate that these null findings cannot be interpreted to indicate no relationship between perchlorate exposure and thyroid function.

(4) Relies on a PBPK model parameterized with weak data. It is discouraging that EPA went to the effort of obtaining the code for the Clewell et al. PBPK model and modified it without critically evaluating the data employed to parameterize the model.

Considering these 4 points, it is our opinion that a scientifically valid RfD and HRL will be significantly lower than that the current proposal. Moreover, the data are available to scientifically defend a return to EPA's draft RfD of 2002.

Response: EPA acknowledges and thanks you for providing comments. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to

regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Carol Bigelow
Commenter Organization: University of Massachusetts
EPA Document ID: EPA-HQ-OW-2008-0692-1427
EPA Comment ID: 20628
EPA Comment Code: 2500

Comment: Thyroid hormone insufficiency in the neonate and infant leads to irreversible health consequences. Defects in thyroid hormone regulation negatively impact brain development and may contribute to a cluster of irreversible neurological defects that includes autism. This literature - completely ignored by EPA's analysis - is compelling public health rationale for regulating perchlorate exposure.

Perhaps the best examples of infants' unique sensitivity to thyroid hormone insufficiency are the studies of infants with congenital hypothyroidism (CH) (for review, see (Zoeller and Rovet, 2004)). These studies are particularly useful because subjects are under continuous medical surveillance so there is good documentation of the relationship between endogenous thyroid hormone, levels of hormone supplementation, and developmental outcome (Heyerdahl and Oerbeck, 2003). The neuropsychological outcome of children diagnosed with CH at birth is associated with both the severity of CH and early treatment factors (how soon T4 was administered, starting dose and serum T4 levels during the first two years of life). These T4 parameters were highly correlated with verbal IQ at age 20, and children with CH who ultimately completed high school had a significantly higher T4 starting dose than those who did not (Oerbeck et al., 2003). Strikingly, the difference in mean starting dose between these two groups was a modest 2.1 ug/kg-day. Because iodine represents 65% (w/w) of T4, the amount of iodine associated with that T4 difference was only 1.37 ug/kg-day. Independent studies were consistent in their findings. In Selva et al. (2002) and Selva et al (2005), a difference in starting dose of only 12.5 μg/day (8.13 ug/day iodine equivalent or 2.3 ug/kg/d) was associated with a significant difference in full scale IQ of 11 points (Selva et al., 2002; Selva et al., 2005). Thus, small differences in available thyroid hormone (and the iodine associated with it) during the first few weeks of life can have significant lifetime consequences including, especially, reduced IQ.

In addition, the experimental literature clearly demonstrates that specific neurodevelopmental events are irreversibly damaged by marginally-low thyroid hormone. These include neuronal migration (Lavado-Autric et al., 2003; Auso et al., 2004), synaptic function (Gilbert and Sui, 2006, 2008), white matter development (Sharlin et al., 2008), and the development of nodular heterotopias (Goodman and Gilbert, 2007). Each of these developmental events will have cognitive and neurological sequelae in humans.

In its unsupported reliance on the NAS report of 2005 (NRC, 2005), EPA did not focus their analysis on the relevant vulnerable groups, the neonate and infant. In this regard, EPA failed to employ one of the largest, and critically relevant, data sets relating thyroid hormone to health consequences - that of neonates and infants (see (Chan and Rovet, 2003; Zoeller and Rovet, 2004)). The superficial reference EPA makes to the infant is wholly inadequate in the current version of this document and should take into consideration the issues developed above and expanded previously (Ginsberg et al., 2007). In addition, EPA should review the issue of genetic factors that may impact individual sensitivity to perchlorate exposure (Scinicariello et al., 2005). Due consideration to this published literature will dramatically change the EPA's analysis.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Carol Bigelow
Commenter Organization: University of Massachusetts
EPA Document ID: EPA-HQ-OW-2008-0692-1427
EPA Comment ID: 20631
EPA Comment Code: 2500

Comment: Also lacking in the science presented in docket ID No. EPA-HQ-OW-2008-0692 are the power considerations necessary to inference making that is precise. Indeed, several of the studies relied upon by the US EPA lacked the statistical power needed to rule out a non-null association.

EPA has failed to address key questions regarding the studies it uses to defend ignoring the CDC study. Specifically, given the known variability in measures of thyroid function (Andersen et al., 2002; Andersen et al., 2003) and maternal, infant and delivery factors on neonatal and thyroid status (Herbstman et al., 2008a; Herbstman et al., 2008b), to what extent do epidemiological studies exploring the relationship between perchlorate and thyroid function provide reliable evidence of a null relationship? Andersen et al. (Andersen et al., 2003) discuss the sources of variability in measures of thyroid hormone in adults. These are critical considerations to employ in estimating the ability of epidemiological studies to identify relationships of interest between perchlorate and thyroid function. Moreover, Andersen et al. (2002) found that to identify the homeostatic set-point within 5% precision required 85 individual measures of TSH and 25 of total T4. Given this degree of variation, studies comparing average measures of thyroid function and proxy measures perchlorate exposure have little - if any - ability to identify relationships of interest. Therefore, EPA is required to determine which of the epidemiological studies it used in its analysis had the potential to identify

a relationship between perchlorate exposure and thyroid function, and the degree to which null findings are meaningful.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Brie Brigham
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1436
EPA Comment ID: 20894
EPA Comment Code: 2500

Comment: Perchlorate interferes with iodine uptake in the thyroid gland, leading to low thyroid production, termed hypothyroidism. Perchlorate also impedes the thyroid's ability to produce hormones that foster mental and physical development. Robert Zoeller, a professer at the University of Massachusetts who specalizes in thyroid hormone and brain development stated a reduction in thyroid function in fetuses, newborns, and children could translate to a loss of IQ and an increase in behavior and perception problems. Zoeller also stated that the impacts are irreversible, meaning that even small changes in thyroid functions in early life have impacts on functioning through high school and even into people's early twenties.

Response: EPA acknowledges and thanks you for providing additional information related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Caroline Baier-Anderson, PhD
Commenter Organization: Environmental Defense Fund

EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20944
EPA Comment Code: 2500

Comment: New data indicate that increases in TSH, resulting from decreased circulating thyroid hormones, may also increase perchlorate uptake in the thyroid (Tran et al. 2008).

There are critical windows in fetal, neonatal, and infant development where insufficient thyroid hormones are associated with disruptions in neural development leading to cognitive deficits (Woodruff et al. 2008). The NIS is expressed in the placenta, and a recent study has shown that the NIS can transport perchlorate across the placental barrier and lead to increased exposure to the developing fetus (Tran et al. 2008). It is therefore not unreasonable to suggest that perchlorate transport could be exacerbated by low maternal thyroid hormones that stimulate TSH release, which enhances perchlorate transport into the maternal thyroid, and across the placental barrier (Tran et al. 2008). Several studies have shown that even moderate maternal thyroid hormone insufficiency during these critical developmental windows can have a significant and lasting impact on the child, such as reduced IQ scores (Haddow et al. 1999; Morreale de Escobar et al. 2000; Pop et al. 2003). Comprehensive studies of the impact of perchlorate exposure on children of mothers that have low iodine intake are lacking, and increased research in this area is needed.

This problem is complicated by extensive individual variability such that the current ranges used to assess thyroid health may not effectively identify adverse downstream effects (Anderson et al. 2002). Therefore, the focus on modulation of thyroid hormones rather than clinical endpoints may be warranted because important concerns have been raised regarding the current method used to assess thyroid health, specifically comparison of thyroid hormone levels with pre-defined acceptable ranges. In their study Anderson et al conclude: "we found that individual reference ranges for serum T3 and T4 are about half the width of population based reference ranges. Hence, a test result within the laboratory reference limits is not necessarily normal for the individual." This is consistent with, and may help explain the observation discussed above, that even small decrements in maternal T4 that do not constitute clinical hypothyroidism can impact neurological development in children. In fact, there is evidence that hypothyroidism is prevalent in the US, yet often undetected, and untreated (Aoki et al. 2007)

An additional complicating factor is that Centers for Disease Control and Prevention (CDC) data indicate that over thirty percent of US women are not obtaining sufficient iodine (Caldwell et al. 2005). Insufficient iodine intake can predispose the thyroid gland to adverse effects of endocrine disrupters especially under phases of vulnerability during development and under adaptive challenges during diseases (Kohrle 2008). Thus, insufficient iodine intake could increase vulnerability to perchlorate. Insufficient iodine intake, assessed by comparing urinary iodine excretion to World Health Organization standards for iodine sufficiency, can increase sensitivity to uptake inhibition by perchlorate.

These major factors described above and summarized below present a clear case that perchlorate exposure poses a significant health risk in the US:

* The principle mode of action of perchlorate is inhibition of iodide uptake by the thyroid, * More than thirty percent of US women are not getting sufficient iodine, * Hypothyroidism is prevalent in

the US population, yet often undetected and untreated, * Neurological damage can occur in babies born to with subclinical hypothyroidism.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20990
EPA Comment Code: 2500

Comment: 2. EPA is ignoring data that demonstrates setting an MCL for perchlorate will provide a meaningful opportunity for health risk reduction

A. Data since the NRC report suggest that perchlorate is even more hazardous than previously thought.

Even based on older studies, EPA acknowledged in its preliminary determination that perchlorate may have adverse health effects. More recent studies show that the effects on humans may be even more dangerous than EPA thought.

Data showing that perchlorate is actively transported into mammary epithelial cells by the sodium iodide symporter (NIS), resulting in an accumulation of perchlorate in breast milk[FN23: Dohan, O, C Portulano, C. Basquin, A Reyna- Noyra, LM Amzel, and N Carrasco. 2007. The Na+/I-symporter (NIS) mediates electroneutral active transport of the environmental pollutant perchlorate. PNAS 104(51):20250-20255.][FN24: Dasgupta, P. K., Kirk, A. B., Dyke, J. V., and Ohira, S.-I. (2008). Intake of Iodine and Perchlorate and Excretion in Human Milk. Environ. Sci. Technol. 42, 8115-8121. Docket HQ-OW-2008-0692 NRDC comments on perchlorate HRL] suggests that perchlorate may not only inhibit iodide accumulation in maternal milk but also could be transferred through milk to the nursing infant where it would be predicted to inhibit iodide uptake in the infant's thyroid gland. The NIS also is found in the placenta and based on this new research, it seems likely that perchlorate is actively transported across the placenta. Because the fetus and developing infant require adequate iodide for thyroid hormone function, any determination of a safe level of exposure to perchlorate should take into account this mode of action for perchlorate toxicity.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 21002
EPA Comment Code: 2500

Comment: C. Sensitive populations not protected by HRL

A related study estimates perchlorate doses that correspond to urinary perchlorate excretion (hereinafter referred to as "Blount (2007)").[FN62: Blount BC, Valentin-Blasini L, Osterloh JD, Mauldin JP, Pirkle JL. Perchlorate exposure of the US Population, 2001-2002. J Expo Sci Environ Epidemiol. 2007 Jul;17(4):400-7. Epub 2006 Oct 18.] These calculations are feasible because perchlorate is not metabolized and has a short half-life of approximately 8 hours[FN63: Ibid.]. Blount (2007) showed that the adjusted geometric mean for perchlorate exposure in women was 0.059 ug/kg-day, and the 95th percentile exposure was 0.215 ug/kg-day. This means that the adverse effects described by Blount (2007) are occurring at perchlorate exposures below the RfD of 0.7 ug/kg- day, with the logical inference being that the proposed HRL will not protect sensitive subpopulations.

A study by Ginsburg et al.[FN64: GL Ginsburg, DB Hattis, RT Zoeller, and DC Rice. 2007. Evaluation of the U.S. EPA/OSWER preliminary remediation goal for perchlorate in groundwater: Focus on exposure to nursing infants. Environ Health Perspect. 115(3):361-369. http://www.ehponline.org/members/2006/9533/9533.html] published since the NRC review found that, "drinking-water perchlorate must be < 6.9 ug/L to keep the median, and < 1.3 ug/L to keep the 90thpercentile nursing infant exposure below the RfD."[FN65: GL Ginsburg, DB Hattis, RT Zoeller, and DC Rice. 2007. Evaluation of the U.S. EPA/OSWER preliminary remediation goal for perchlorate in groundwater: Focus on exposure to nursing infants. Environ Health Perspect. 115(3):361-369.] Based on both exposure and toxicity information, and data on sensitive populations, the proposed HRL, which is twice as high as the limit proposed by Ginsberg et al, will leave significant portions of the population at risk.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary

determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21057
EPA Comment Code: 2500

Comment: This year, the ATSDR released its Toxicological Profile for Perchlorates (2008) as new data have become available since the last profile of perchlorates in 2005. As a part of their review, ATSDR derives minimum risk levels (MRLs) using available peer reviewed information. MRLs "...are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration for a given route of exposure. An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. MRLs are based on noncancer health effects only and are not based on a consideration of cancer effects. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean-up or action levels" (ATSDR, 2008). Considering the NRC report along with new studies published since the NRC report, "ATSDR has adopted the EPA's chronic RfD recommended by the NRC (2005) for the chronic MRL" (ATSDR, 2008).

ATSDR based their MRL on the same most sensitive population, pregnant women and their fetuses, although they also discussed other sensitive populations, preterm and nursing infants. They also state that their decision "...was made after a careful evaluation of the NRC report and of studies that have been published after the NRC (2005) report. The results from newer studies do not change the bottom-line recommendation" (ATSDR, 2008).

The ATSDR Toxicological Profile for Perchlorates was peer reviewed and made available for public comments. "The expert peer reviewers on April 18, 2007 concluded that the MRL should still be based on the RfD as recommended by the NRC Panel Report (2005) given the research data available at the time of the 2007 peer review" (ATSDR, 2008).

Based on the traditional and foundational approach used in science, the weight of evidence-or the number of well conducted studies in humans and animals with appropriate dose-response information-supports EPA's decision not to establish a NPDWR. As shown in the assessment by the NRC in 2005 and the subsequent literature published since then, including the ATSDR Toxicological Profile, the weight of evidence shows that,

* inhibition of iodide uptake in the thyroid gland is a key biochemical event, * the inhibition of iodide uptake is not an adverse effect, * there are doses of perchlorate below which inhibit iodide uptake in healthy adults, * the dose of perchlorate that might be sufficient to cause an adverse effect is as sustained exposure greater than 0.4 mg/kg-d (NRC, 2005), and * there are natural occurring agents, such as thiocyanate and nitrate, that also effect iodide uptake in the thyroid gland.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21060
EPA Comment Code: 2500

Comment: The weight of evidence shows that the fetal brain is more sensitive to hypothyroidism than the neonate or infant brain (Boelaert and Franklyn, 2005). Breast milk concentrations of perchlorate have been measured at levels greater than the HRL (Kirk et al., 2005; Pearce et al., 2007b). However, the RfD assumes that if a person consumes 15 ppb of perchlorate not just once, but every day for a lifetime, they will be consuming a concentration of perchlorate that is not anticipated to cause an adverse effect. Furthrermore, a HRL, MRL, PHG[FN1: A Public Health Goal, or PHG, is the State of California's acceptable level of a chemical in drinking water that is not expected to cause an adverse effect if consumed every day for a lifetime.], RfD, etc. are not bright lines above which health effects would be expected to occur. As noted with perchlorate, an RfD based on a no effect level for a non adverse effect in humans with an additional 10-fold uncertainty ("safety") factor provides a health protective approach. The development of a value lower than the RfD will only increase the level of caution. Therefore, if an infant consumes one dose of perchlorate that is greater than the RfD, it is not expected to be any more harmful than a lesser dose. Lastly, a solely breast fed infant will not have exposures through other media.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in

drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21061
EPA Comment Code: 2500

Comment: II. KEY SCIENTIFIC STUDIES PUBLISHED SINCE 2005

Since the publication of the NRC report in 2005, several studies have been published that support the conservative nature of the current EPA RfD. Overall, these studies demonstrate that perchlorate is a ubiquitous chemical in the environment, food, and the human body. In a recent study by Blount et al. (2007), all samples of urine measured had low, but detectable concentrations of perchlorate. The sources of perchlorate appear to be both natural and anthropogenic. There is an increasing body of literature demonstrating that much of the environmental perchlorate may be natural or due to non-point sources (DasGupta et al., 2005; SERDP, 2005; DasGupta et al., 2006; Rajagopalan et al., 2006).

[Text Box: The weight-of-evidence of human and animal studies that include sufficient dose-response data, show that possible adverse health effects are several orders of magnitudes above environmentally-relevant levels of perchlorate and that the current RfD is a conservative toxicity guideline value such that contaminants present in drinking water at or below the HRL of 15 ppb would pose no significant health risk to the most sensitive individuals who consume the water on a daily basis over a lifetime.]

Despite the widespread low levels of perchlorate in the environment, studies have not demonstrated an adverse effect due to perchlorate exposure. The NRC report states,

"The committee emphasizes that inhibition of iodide uptake by the thyroid has been the only consistently documented effect of perchlorate exposure in humans. The continuum of possible effects of iodide-uptake inhibition caused by perchlorate exposure is only proposed and has not been demonstrated in humans exposed to perchlorate (with the exception that in patients with hyperthyroidism doses of 200 mg daily or higher may reduce thyroid secretion). More important, the outcomes at the end of the continuum are not inevitable consequences of perchlorate exposure." (NRC, 2005)[FN2: The noted dose of 200 mg/d is a conservative therapeutic value. When use of perchlorate to treat hyperthyroidism was common, doses of 400 mg/d were commonly prescribed, but were found to be slow to control thyrotoxicity and doses needed to be repeated 4 to 5 times/d, due to the rapid excretion of the drug. Although it still took an average of 9.4 weeks, doses of up to 2000 mg/d were given to reduce hyperthyroidism to a remission state (Wolff, 1998).]

The new studies contribute to an already well developed database, adding more studies that are consistent with previous analyses. Furthermore, additional studies that are consistent with the literature also reduces uncertainty (reducing "what we do not know"), thereby reinforcing that the current RfD for perchlorate is both conservative and health protective. Thus, perchlorate concentrations equal to or above the EPA-recommended HRL of 15 ppb in water would also be conservative and health protective for sensitive populations.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21062
EPA Comment Code: 2500

Comment: A. Environmental Studies

EPA states: "If adequate human studies (confirmed for validity and applicability) exist, these studies are given first priority in the dose- response assessment, and animal toxicity studies are used as supportive evidence." and "If adequate human data are available, this information is used as the basis of the RfD (EPA, 1989). The scientific studies regarding perchlorate and health are predominately based upon human data, with a range of parameters and dose-response data. The types of human studies are clinical, occupational, or ecological. To date, there is only one epidemiological study which measures perchlorate exposures and outcomes in pregnant women and neonates (Tellez et al., 2005). In contrast to ecological studies measuring collective exposures and outcomes, an epidemiological study measures individual exposure and outcome. There are also some well designed animal studies that have contributed to the health effects database. Many of these studies investigate the relationship between perchlorate exposure and adverse outcomes among especially vulnerable groups. In addition to the clinical studies reviewed by NRC, epidemiological studies are valuable in exploring the health effects due to perchlorate in a chronically exposed genetically-diverse population that includes the population of concern (pregnant women and their fetuses).

In the EPA notice, several of these association studies were taken together, leading EPA to conclude that the results of "...studies of the effects of perchlorate exposure on hormone levels have been mixed" (p. 60266), citing Amitai et al. (2007) showing no effects and Blount et al. (2006) identifying

hormonal changes (although none were outside normal ranges). However, when the strength of the study design is taken into consideration, the weight-of-evidence demonstrates that the current RfD is a conservative toxicity guideline value such that contaminants present in drinking water at or below the HRL of 15 ppb would pose no significant health risk to the most sensitive individuals who consume the water on a daily basis over a lifetime.

Response: EPA acknowledges and thanks you for providing additional information related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21070
EPA Comment Code: 2500

Comment: In a peer-reviewed letter to the editor of Thyroid, Gibbs and Van Landingham (2008) reviewed data from their previously published study (Tellez et al., 2005), and showed that in a cohort of pregnant women in Chile, the data do not support the association between environmental perchlorate exposure and changes in thyroid hormones and are consistent with the recent negative findings by both Pearce et al. (2007b) and Lamm et al. (2008), both presented at the Seattle SOT meeting.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Michael Girard

Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21074
EPA Comment Code: 2500

Comment: B. Occupational or Clinical Studies

i. Braverman et al. (2005)

This study included 29 workers exposed for at least 1.7 years in an ammonium perchlorate plant and 12 unexposed volunteers; variables measured in the study included serum perchlorate, thiocyanate, nitrate, total T4, Free T4, total T3, Tg, and TSH; RAIU; and urinary iodine and perchlorate taken after 3 days off or 3 days working. The authors estimated that "half of the workers experienced average ClO4- doses in excess of 0.33 mg/kg-shift over the year preceding this study." They found that there was a decrease in RAIU, but no change in thyroid hormones compared to unexposed controls. There was a slight increase in T3, T4, and free T4 after 3 days working compared to 3 days off. Again, the NRC committee has stated that "The committee does not think that transient changes in serum thyroid hormone or TSH concentrations are necessarily adverse effects" (NRC, 2005). The RAIU dose response curve the authors found was consistent with that of Greer et al. (2002).

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21075
EPA Comment Code: 2500

Comment: ii. Braverman et al. (2006)

In an effort to study the thyroidal effects of a prolonged (six months) exposure to low perchlorate levels in humans, Braverman et al. exposed 13 healthy volunteers to 0, 0.5, or 3.0 mg/d of potassium perchlorate and measured urinary perchlorate levels, radioactive iodine uptake and serum T3, free T4, TSH and Tg concentrations. The 0.5 and 3.0 mg/d doses are equivalent to 250 and 1500 ppb, respectively, assuming a daily water ingestion of 2 liters. The authors concluded that perchlorate at

doses of up to 3 mg/day for six months "...had no effect on thyroid function, including inhibition of thyroid iodide uptake as well as serum levels of thyroid hormones, TSH and Tg" and, "...there was no significant change in the thyroid RAIU during perchlorate administration." (emphasis added)

This study was similar to Greer et al. (2002), but for longer exposures. The doses were 0.5 and 3.0 mg/d and the exposures were for six months. This study also did not restrict or control for dietary intake (Crawford-Brown et al., 2006).[FN6: "If one assumes that the individuals in the study by Greer et al. (2002) were exposed to the same background levels of perchlorate as the rest of the U.S. population (there is nothing in their diets or in the study design to preclude this), then no further RSC adjustment is needed to reflect total exposures via all routes because the risk coefficient from the study already reflects the incremental risk from ingestion of perchlorate in water above and beyond the contributions to perchlorate exposure via the other routes" (Crawford-Brown et al., 2006).] Therefore, the doses administered as part of this study were in addition to the background levels of perchlorate ingested-the impact of dietary iodine intake was not accounted for. The study would have benefited from a larger sample size; however, data from the 14-day Lawrence et al. (2000, 2001) studies, and the Greer Study support the results reported by Braverman et al. These studies all support the NOEL determined by Greer et al. (2002), and relied upon by the NRC as the basis for its recommended RfD.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Ladd Larry
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0037
EPA Comment ID: 28337
EPA Comment Code: 2500

Comment: Larry Ladd says regulate. Data gap 1: Chronic effects of ClO4- in the skin. Half-life is longer than in the thyroid or the blood (Yu et al 2002, pubmed id 12140178). No discussion of how ClO4- causes drug-induced lupus and erythema nodosum (Beickert & Heinicke 1968, pmed id 4181403), the role I- sometimes plays in relieving erythema nodosum (Boyd 2007, pmed id 17618179; Sterling & Heymann 2000, pmed id 11004629), or similar ailments caused by chaotropic anions such as iododerma, bromoderma, and bromism. Data gap 2: Variation in infant renal excretion of ClO4-. If pendrin is important in ClO4- as well as I- excretion (for I- see Kim et al -- pmed id 19605545) , expect infant with acidosis (including low HCO3- from chronic diarrhea?) to retain more ClO4- (Frische et al 2003, pmed id 12556366). Data gap 3: Chaotropic effects

preventing immuno- coagulation such as opsonization of B-19 parvovirus by IgG (Chehadeh et al 2009, pmed id 19450862, with the parvovirus outbreaks in Dharan after Patriot missile deployment, Mallouh & Qudah 1995 pmed 7715986 [corrected per commenter's request, see docket ID 08090372] and western Pennsylvania during peak fireworks production, Beigi 2008, pmed id 18464909 in mind); opsonization of staph by pentraxin 3, which is dependent on a cysteine array (Holland et al, 2009 pmed id 19054079; Inforzato et al 2008, pmed id 18223257); defensin adhesion to coccidoidomycosis, H. pylori, mycobacteria, and influenza, which is also dependent on a cysteine array vulnerable to changes in salinity (Chandrababu et al 2009, pmed 19480463). Analysis is lacking of NIS and SCN- in the airway (Fragoso et al 2004 pmed id 15345749; Pedemonte et al 2007 pmed id 17404297; Wang et al 2006 pmed id 17142773) and nitrosation in the gastrointestinal tract (Suzuki et al 2003 pmed id 12940440). In regards to humoral immunity, you need to evaluate the thickening of rat pup corpus callosum recorded in York et al 2005 (pmed id 16393938) with the migration paths of cd34+ stem cells within the rat brain (Jendelova et al 2005 pmed id 15929552).

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Steve Lamm
Commenter Organization: Consultants in Epidemiology and Occupational Health, LLC (CEOH)
EPA Document ID: EPA-HQ-OW-2009-0297-0654
EPA Comment ID: 28487
EPA Comment Code: 2500

Comment: Is there an adverse neurodevelopmental effect with perchlorate exposure in an iodine-sufficient population?

Are moderate perchlorate exposures associated with adverse neurodevelopmental or cognitive outcomes? The ecological study Chang et al. (2003) showed there was no increase in ADHD or autism or decrease in fourth-grade performance with perchlorate levels up to 24 ug/L in Nevada. This study was done in the US iodine-sufficient population without distinguishing those with low iodine levels. The Lamm and Dohmland (1999) study found no increased incidence rate of congenital hypothyroidism in California and Nevada counties with perchlorate drinking water levels in the range of 4-16 ug/L.

Are moderate perchlorate exposures associated with lower levels of neonatal thyroxine (or elevated neonatal TSH)? Li et al. (2000a) and Li et al. (2000b) showed no effect on neonatal thyroxine levels

or neonatal TSH levels, respectively, from environmental exposures to perchlorate that ranged up to 15 ug/L, also in Nevada.

At background levels of perchlorate exposure, are lower levels of neonatal thyroxine in the physiological range associated with adverse neurodevelopment outcome including cognition? Soldin et al. (2002) and Soldin et al. (2003) showed in case-control studies that neither childhood ADHD nor pediatric neurobehavioral diseases, respectively, were impacted by variations in neonatal thyryroxine levels. These studies were conducted in Washington, DC, whose water supply has no known perchlorate contamination. Recently, Oken et al. (2009) have demonstrated from a prospective cohort study of 500 children in Massachusetts that cognitive test scores at ages 6 month and 3 years were not associated with lower neonatal thyroxine levels. Further, newborn thyroxine levels were not associated with maternal measures of thyroid function (thyroxine, TSH or thyroperoxidase antibody levels).

Are background perchlorate exposures associated with adverse maternal thyroid function measures? Pearce et al. (2007) presented results demonstrating that maternal thyroid function is not affected by environmental perchlorate exposure, based on urinary perchlorate levels of first trimester pregnant women in Cardiff, UK, where the population is mildly iodine-deficient (i.e, median = 90 ug/L). Pearce et al. (2008) expanded the study in Turin, Italy, asking the same question for an iodine-deficient population.

Pearce et al. (2008) showed among 526 first trimester pregnant women in Turin, Italy, an iodinedeficient population with a median urinary iodine value of 50 ug/L, that there was no association between urinary perchlorate levels and free T4 levels ($r2<0.0001$, $p = 0.9$) or serum TSH ($r2=0.002$, $p = 03$). Their results were the same when they limited their analysis to the 433 women with urinary iodine values less than 100 ug/L. They concluded that "These results, from the largest sample to date of women with low urinary iodine values, do not support the findings reported in the U.S. that similar levels of perchlorate exposure increase serum TSH and lower serum T4 in women with urine iodine concentrations < 100 ug/L."

The Pearce et al. (2008) study is a direct test of the hypothesis raised by the Blount et al. (2006) study, and, in particular for the population of great interest, pregnant women. This study is currently undergoing peer-review for the medical literature.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Steve Lamm
Commenter Organization: Consultants in Epidemiology and Occupational Health, LLC (CEOH)
EPA Document ID: EPA-HQ-OW-2009-0297-0654
EPA Comment ID: 28488
EPA Comment Code: 2500

Comment: In summary, the published studies demonstrate no adverse effect on infant thyroidal or neurodevelopmental health from perchlorate exposures up to 16-24 ug/L and no effect on neurodevelopmental or cognitive health with variations in normal neonatal thyroxine levels. Maternal thyroidal function has not been affected by background perchlorate levels either among UK women in a mildly iodine-deficient population or among Italian women in an iodine-deficient population, even those Italian women with urinary iodine levels less than 100 ug/L. These results challenge the interpretation of the Blount et al. (2006) analyses of the NHANES 2001-2002 cross-sectional database.

These comments are respectively submitted. I would be happy to supply any reference material that is not already in the record, and I keep myself open to participate in any further scientific discussions on these matters.

Cordially, Steven H. Lamm, MD, DTPH Consultants in Epidemiology and Occupational Health, LLC. 3401 38th street, NW #615 Washington, DC 20016 202/333-2364 Steve@CEOH.com

Associate in Department of Health Policy and Management Johns Hopkins University-Bloomberg school of Public Health Assistant Professor, Department of Pediatrics (Epidemiology) Georgetown University

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Attached are copies of the citations Rasmussen and Andersen cited in my submission: Comment Tracking Number: 80a3e697. [See PDF docket ID EPA-HQ- OW-2009-0297-0655; note this is copyrighted materials]

Attached are copies of the citation by Laurberg cited in my submission: Comment Tracking Number: 80a3e697. [See PDF docket ID EPA-HQ-OW-2009-0297-0656; note this is copyrighted material]

Attached are copies of the citation by Oken cited in my submission: Comment Tracking Number: 80a3e697. I hereby submit to your record by reference the three submissions we made to the record of the EPA Office of the Inspector General on March 10, 2009. That includes the Vanderver and Lamm papers and the two Lamm abstracts. [See PDF docket ID EPA-HQ-OW-2009-0297-0657; note this is copyrighted material]

Attached are copies of the citations Pearce 2007 and Pearce 2008 cited in my submission: Comment Tracking Number: 80a3e697. [See PDF docket ID EPA-HQ- OW-2009-0297-0658]

These is the cover letter to our submission on Vanderver March 10, 2009 to the EPA OIG and the article. [See PDF docket ID EPA-HQ-OW-2009-0297-0659]

Here are submission 2 to the EPA-OIG March 10, 2009. [See PDF docket ID EPA-HQ- OW-2009-0297-0660]

This is submission 3 to the EPA_OIG concerning iodine supplementation. This is the cover letter. It will not accept the abstract, so I will send it separately. [See PDF docket ID EPA-HQ-OW-2009-0297-0661]

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: James D. Taft
Commenter Organization: Association of State Drinking Water Administrators
EPA Document ID: EPA-HQ-OW-2009-0297-0525
EPA Comment ID: 28503
EPA Comment Code: 2500

Comment: EPA discusses but does not ask for any specific comments related to studies published since they adopted the RfD for perchlorate. ASDWA does not have any additional research to offer and simply suggests that EPA review the available, peer reviewed, scientific data.

Response: EPA will continue to evaluate the available science related to perchlorate as the Agency makes a regulatory determination for perchlorate.

Commenter Name: Jonathan Borak
Commenter Organization: Yale School of Medicine
EPA Document ID: EPA-HQ-OW-2009-0297-0209
EPA Comment ID: 28510
EPA Comment Code: 2500

Comment: Blount et al. and Steinmaus et al. adopted the 100 ug/L level for their studies because it is the WHO/UNICEF/ICIDD criterion for iodine sufficiency (16). However, that level has been recommended as a benchmark for evaluating the median spot urinary iodine level of populations; it has not been advocated for determining iodine sufficiency in individuals. It is not a useful benchmark for individuals because, as described below, individuals demonstrate significant variability of urinary iodine. Many individuals with sufficient iodine intake have spot urine levels <100 ug/L level from time to time.

Urinary iodine levels generally reflect dietary iodine intake over the prior 12-24 hour period, with peaks occurring about 8-12 hours after major meals, thus variations in day-to-day diet can lead to marked day-to-day variations in spot urine iodine (17). Significant day-to-day variations have also been documented in subjects with controlled dietary iodine intake.

For example, six adults studied for 30 days at the NIH Clinical Center were given a diet that provided a constant daily iodine intake (18). Following a six- day stabilization period, daily 24-hour urine specimens were collected for iodine measurements. Day-to-day coefficients of variation (CV) for 24-hour iodine excretion were calculated for each of two successive 12-day periods. Among individual subjects, CVs ranged from 7%-24.1%. Thus, even under controlled conditions, constant diet and 24-hour urine collection, there was substantial day-to-day variability of iodine excretion.

Greater variability was seen in studies that did not restrict subjects' diets and iodine intake.

Rasmussen et al. measured iodine levels in 24-hour urine samples collected on four consecutive days from each of ten subjects whose diets and iodine intake were not controlled. For individuals, day-to-day urinary iodine levels varied up to three-fold (19).

Burgi et al. collected morning urine samples from eleven subjects on 21 consecutive days. Diets and iodine intake were not controlled. For individuals, day-to-day CVs ranged from 15%-75%; the average day-to-day CV for the group was 39%. Results from individual subjects demonstrated hectic day-to-day variability (20).

Andersen et al. measured urinary iodine in 15 men sampled monthly for 12 months. Diets and iodine intake were not controlled. Twelve-month averaged urine levels for individuals ranged from 29-81 mg/L, but individual monthly urine levels ranged from 10-260 mg/L. The CVs calculated for each subject's 12 monthly samples ranged from 20.1%-70.5 % (21).

In addition, urinary iodine excretion follows diurnal and seasonal cycles. Higher urine iodine levels are generally found in morning samples and wintertime samples (17).

Because of such day-to-day variations in urine iodine excretion, studies that consider only isolated spot urine levels report significantly greater dispersion of individual urine levels than do studies which average urine levels over time. In other words, isolated spot urinary iodine levels are imprecise reflections of an individual's iodine sufficiency.

More generally, isolated urinary iodine levels provide little useful information about the long-term iodine nutrition of an individual. For example, consider the views of the National Academy of Clinical Biochemists (17):

"In most circumstances the determination of urine iodine provides little useful information on the long-term iodine status of an individual, since the results obtained merely reflect recent dietary iodine uptake."

For such reasons, dividing a population into two groups solely on the basis of a single spot urinary iodine level, as in the Blount and Steinmaus studies, will almost certainly lead to significant exposure misclassification. Blount et al. and Steinmaus et al. recognized that possibility, but argued that such misclassification would be "random error (not bias)" and thus "nondifferential and therefore likely to bias estimates of association toward the null, not toward the positive effects" (14). That statistical argument is valid for nondifferential misclassification of binary exposure categories, but it is not necessarily valid for more complex sorts of misclassifications:

"Contrary to popular misconceptions, however, nondifferential exposure or disease misclassification can sometimes produce bias away from the null." (22)

The Blount et al. study classified individuals based on single spot urine levels of iodine and perchlorate; Steinmaus et al. also included a spot urine level for thiocyanate. Misclassifications would not have been simple and binary. Still greater complexity and potential bias arise from the fact that day-to-day variations of iodine and perchlorate intake do not vary randomly from each other. For example, the FDA Total Diet Study (23) documents that some food groups (e.g., dairy) are major sources of both iodine and perchlorate, while others (e.g., grains, vegetables) are rich in only one or the other. Thus, day- to-day dietary variations may result in either strongly positive or strongly negative associations between these two anions. In any event, their relationship is unlikely to be random. Further complicating analytical assessment and interpretations is the fact that iodine and perchlorate have different serum half-lives and different urinary excretion rates (11,12).

It is not reasonable to minimize the importance of such misclassification by reliance on "popular misconceptions". Even more complex misclassification bias and confounding can be expected when other 'NIS stressors' (e.g., thiocyanate and nitrate) are measured in isolated spot urines and included in the analysis. For such reasons, cross-sectional data based on isolated spot urine samples must be used with caution when inferring causation and estimating the magnitude of potential interactions.

For the same reasons, isolated spot urine levels should not be used to characterize the proportion of a population deemed "iodine deficient"; doing so will overestimate the number of "deficient" individuals. That concern was also expressed by the NAS Committee to Assess the Health Implications of Perchlorate Ingestion ("NAS Committee") (24):

"... the distribution of iodide values measured in spot urine samples is broader than values measured repeatedly in individual subjects (21); this leads to overestimation of the number of subjects with both low and high values."

The NAS Committee also raised concerns about the over-interpretation of NHANES spot urine iodine data to suggest that significant numbers of young adults (including pregnant women) had significant iodine deficiency because their spot urine levels were <100 ug/L (24)

"Furthermore, among people 15-44 years old, including pregnant women, there were no differences in serum TSH and T4 concentrations between those with urinary iodide values less than 50 ug/L and those with higher values (25); apparently, the iodide intake in the former group was not low enough to cause a fall in T4 secretion."

In reviewing these concerns, the OIG concluded that there was "significant uncertainty" when NHANES data for isolated spot urinary iodine were used as the basis for determining iodine sufficiency in pregnant women:

"these results do represent a significant uncertainty in the science concerning this public health issue (i.e., what portion of the U.S. pregnant women population are moderately or mildly iodide deficient?)." (13)

In summary, use of simultaneous measurements of iodine, perchlorate and other NIS stressors in isolated spot urine samples to characterize cross-sectional populations can be expected to result in significant misclassification that may bias associations toward or away from the null. Likewise, they are likely to overestimate the numbers of individuals at the extremes of the population distribution. Analytical findings and population characterizations based on such testing are likely to introduce significant uncertainty in regulatory determinations that rely upon them.

Thank you for this opportunity to comment upon and contribute to your regulatory determination for perchlorate.

Yours truly, Jonathan Borak, MD, DABT, FACP, FACOEM Clinical Professor of Epidemiology and Medicine Yale School of Medicine

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Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Shannon Cunniff
Commenter Organization: Department of Defense (DOD)
EPA Document ID: EPA-HQ-OW-2009-0297-0411
EPA Comment ID: 28529
EPA Comment Code: 2500

Comment: Comment No. 16

Section IV. Consideration of Studies Published Since EPA Adopted the NAS RfD for Perchlorate

Page & Paragraph Page 41891

Comment We would like to call to EPA's attention the new data from the Cao, et al. 2009 perchlorate, thiocyanate, and nitrate manuscript developed in collaboration with the CDC, which the authors believe is the first study of its kind. Individual thyroid function and perchlorate, thiocyanate, and nitrate exposure were directly measured in about 50 infants born at the Children's Hospital of Philadelphia, the Hospital of the University of Pennsylvania, and affiliated clinics, in a study conducted in 2004-2005 where ninety-two full term infants between birth and 1 year of age participated.

In general, the authors' draft manuscript states that associations between TSH and thiocyanate were larger than those between TSH and perchlorate and nitrate. Also, a mixed linear model (one goitrogen exposure at a time) showed that the three goitrogens all had significantly positive associations with TSH and T4. The average urinary thiocyanate level in these infants was almost 50 times higher than average perchlorate level, and thiocyanate was more strongly related to TSH than perchlorate. With all three [goitrogens] modeled simultaneously, all children with higher nitrate and thiocyanate had higher TSH, but higher perchlorate was significant only in children with low iodide.

Suggested Action, Revision and References (if necessary) As EPA continues to evaluate new perchlorate data as stated in the FR announcement this study should be a relevant consideration.

Category* O

Comment No. 17

Section IV. Consideration of Studies Published Since EPA Adopted the NAS RfD for Perchlorate

Page & Paragraph Page 41891

Comment The recent publication describing a model by M. Lorber entitled, "Use of a simple pharmacokinetic model to characterize exposure to perchlorate," Journal of Exposure Science and Environmental Epidemiology (2009) 19, 260-273 was not cited by EPA when evaluating perchlorate modeling alternatives. According to the author:

The primary benefit of these simple models is that they allow for an expanded study of the magnitude and patterns of external exposure. This is a different emphasis than the complex, PBPK models, which are used more to study the internal fate (e.g., dose-to-target organs) and potential health effects of contaminants to which an individual is exposed. ...In short, these simple models are allowing for an expanded and more valid study of external patterns of exposure.

Suggested Action, Revision and References (if necessary) The EPA "in-house" model developed by M. Lorber should be given consideration as appropriate.

Category* S

Comment No. 18

Section V. Next Steps

Page & Paragraph Page 41892

Comment Although EPA indicates that no additional research is needed to make a regulatory decision, Blount et al. (2009), the USEPA OIG perchlorate document (December, 2008), and others have stated that perchlorate, thiocyanate and nitrate from dietary exposure, coupled with low iodine intake merits further research.

Suggested Action, Revision and References (if necessary) We do not want to delay the regulatory process, but encourage further research in these areas to decrease uncertainty associated with perchlorate cumulative risk assessment.

Category* S

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: John P Gibbs
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0636
EPA Comment ID: 28551
EPA Comment Code: 2500

Comment: 2) MORE RECENT STUDIES

Subsequent to the NAS report, Braverman et al 2005 demonstrated the same dose response as Greer for iodine uptake inhibition, among workers with long term perchlorate exposure. There were no demonstrable adverse thyroid effects among the workers in this study or in a previous study at the same location (Lamm et al 1999). Benchmark calculations (Crump & Gibbs 2005) were performed on the data from these two studies as well as with data from the Greer study. The lower 95% statistical confidence limits on benchmark doses estimated from a combined analysis of the two occupational studies ranged from 0.21 to 0.56 mg/kg-day for free T4 index and from 0.36 to 0.92 mg/kg-day for TSH. Corresponding estimates from the short-term clinical study were within these ranges.

Tellez et al 2005 conducted an epidemiological study among pregnant women in Chile and found no impact of perchlorate on maternal thyroid function during pregnancy or on infants at birth. Water perchlorate concentrations ranged from 4ppb to over 100 ppb. Amitai et al 2007 studied neonatal T4 in a region of Israel where perchlorate contamination was found in the public water supply at concentrations far in excess of those documented in the U.S. This study finds no change in neonatal T(4) levels despite maternal consumption of drinking water that contains perchlorate at levels in excess of the Environmental Protection Agency (EPA) drinking water equivalent level (24.5 microg/L). Therefore the perchlorate RfD is likely to be protective of thyroid function in neonates of mothers with adequate iodide intake.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Kay Brothers
Commenter Organization: Southern Nevada Water Authority
EPA Document ID: EPA-HQ-OW-2009-0297-0667
EPA Comment ID: 28699
EPA Comment Code: 2500

Comment: Again, we certainly appreciate the need for modeling when sufficient empirical data do not exist. However, in the case of perchlorate, significant peer- reviewed literature is available that should be considered by EPA before relying on less certain modeling to generate HRLs. **Response:** EPA acknowledges and thanks you for providing comments. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Tom Porta

Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 28749
EPA Comment Code: 2500

Comment: Subject: Docket ID No. EPA-HQ-OW-0297

Reference: Drinking Water: Perchlorate Supplemental Request for Comments (Federal Register / Vol. 74, No. 159 / Wednesday, August 19, 2009 / Notices

The Nevada Division of Environmental Protection (NDEP) provides herein, comments to assist the US Environmental Protection Agency (EPA) in their evaluation of the benefits of establishing a national primary drinking water rule for perchlorate. The EPA is evaluating whether establishing this rule would provide a significant reduction in human health risk by reducing exposure to perchlorate in drinking water. In that context, NDEP comments are provided in response to an August 19, 2009 notice within the Federal Register entitled "Drinking Water: Perchlorate Supplemental Request for Comments", Docket ID No. EPA-HQ- OW-2009-0297.

Comments are arranged in the order presented within the above-referenced Federal Register Notice (Notice). The numerical designation follows that used in the Notice. The attached appendices provide supporting information, along with a reference to guide the reader to specific supporting information. These references provide examples, describe assumptions, and enhance the clarity of the comments. Applicable references are cited throughout the text and appendices, and are listed at the end of this document.

III. Alternative Approaches to Analyzing Scientific Data Related to Perchlorate in Drinking Water:

A. Interpretation of the Physiologically-Based Pharmacokinetic (PBPK) Modeling 4. Request for Comment on Alternative Approaches a. EPA requests comment on using the PBPK model to evaluate the relative sensitivity of various life stages to perchlorate exposure in drinking water.

Comment A.4.a.1: It is inappropriate to use the PBPK model to support a regulatory action because the underlying scientific evidence indicating sensitivity of the fetus and/or neonate is lacking. Additional clinical data are needed to help refine the PBPK model. Data are needed for adults, including pregnant women, and for neonates concerning thyroidal iodine capacity and the effects of sodium-iodide symporter (NIS) upregulation on thyroidal iodine uptake and/or thyroxine levels. Also, additional studies of other adults are needed to evaluate the effects of temporary iodine deficiency and NIS upregulation on perchlorate competitive inhibition of thyroidal iodine uptake and/or free thyroid hormone levels. This additional research would provide useful data to consider in further refining the PBPK model to accurately reflect the effects of iodine deficiency in pregnant women, fetuses and neonates. If the additional clinical data support concerns for relative sensitivity of the fetus and neonate, then a refined and validated PBPK model would be useful.

Comment A.4.a.2: Perchlorate is known to be well absorbed into the human body, and at sufficient doses can act as an inhibitor of iodine uptake into the thyroid due to competition with iodine for the sodium-iodide symporter (NIS) (NRC, 2005). Although this competitive inhibition of NIS is not an adverse health effect, it is apparently the first step in a cascade of events that ultimately reduces the production or release of thyroxine from the thyroid gland into the bloodstream by depleting stored

iodine in the thyroid. However, humans have multiple and redundant mechanisms for maintaining adequate amounts of free thyroid hormones (free thyroxine (FT4) and the active hormone receptor-binding agent, free tri-iodothyronine (FT3)) when diet or environmental agents cause interruption of thyroidal iodine intake or in circulating active hormone levels (Moore, 1984; Moulopoulis et al., 1988). Some of the most prominent homeostatic mechanisms for maintaining adequate levels of circulating FT3 in humans include:

1. NIS upregulation capacity to rapidly (within hours) increase thyroidal iodine uptake; 2. Organification of iodide within the thyroid into thyroglobulin, a protein containing bound T4 subunits that act as a storage pool within the thyroid; 3. Thyroid stimulating hormone (TSH) secretion and thyrotropin releasing hormone (TRH) secretion triggered by various stressors (e.g., cold or fever) or by lowered FT3 in circulation, leading to increased production and secretion of T4 and T3 into the bloodstream; 4. Hypertrophy and/or increase number and volume of thyroid follicular cells (including induction of goiter) with long-sustained TSH stimulation typically from FT3 shortage in circulation; 5. Modulation of thyroid binding globulin (TBG) content in the circulation which alters the storage capacity and free vs. bound hormone balance in the circulation; 6. Modulation of iodide and thyroid hormone excretion via the kidneys, feces, and/or metabolic breakdown of hormones; and 7. Modulation of thyroid function and thyroid hormone distribution by estrogens, human chorionic gonadotropin, leutinizing hormone, and other hormones during pregnancy and lactation.

The human body is recognized to maintain a sensitive and dynamic balance between TSH and FT3, and the thyroid injuries or diseases that significantly alter this dynamic balance (in magnitude and/or duration) have the most clinical importance with respect to thyrotoxicity and adverse health consequences (Moore, 1984; Moulopoulis et al., 1988).

The homeostatic mechanism perhaps most relevant to perchlorate thyrotoxicity in humans and other mammals is the upregulation of NIS when dietary iodine is sufficiently low for an extended period such that thyroidal iodine stores become depleted. Such upregulation of thyroidal NIS leads to an increased number of NIS sites on thyroid follicle cells, which in turn has the impact of increasing iodine uptake and reducing the impact of competitive inhibition by perchlorate and other chemicals with NIS binding capacity such as nitrate, thiocyanate, and bromate. At relatively high doses of NIS competitive inhibitor agents in humans, the most immediate response is NIS upregulation, which restores thyroidal iodine uptake and reduces the effects of most environmental doses of exogenous NIS inhibitors.

The available evidence in studies of rats subjected to subchronic doses of perchlorate indicates solely reversible thyroid effects in perchlorate-treated adults and an important role of homeostatic mechanisms (e.g., NIS upregulation) in effects noted at doses (e.g., 1,000 ug/kg-day) more than 1000-fold higher than the perchlorate reference dose. Paulus et al. (2007) demonstrated that long-term iodine deficiency in rats leads to upregulation of NIS and increased resistance to as much as 5.6 mg/kg-day perchlorate inhibition of thyroidal iodine uptake. The highest dose of 28 mg/kg-day was reported to overwhelm the NIS upregulation in iodine deficient rats, leading to reduced thyroxine levels and corresponding TSH perturbations. Paulus et al. (2007) noted:

"The iodine-deficient animals in this study absorbed twice as much of an administered dose of 1311 into the thyroid as the iodine-sufficient animals (see Table 2). This increase in absorption by the animals on the iodine-deficient diet clearly outweighed other factors affecting absorption. This

increase in absorption is presumably preceded by elevation in release of TSH via the hypothalamus-pituitary-thyroid (HPT) axis, in response to low levels of thyroid hormone. It is known that upregulation of the thyroid by TSH is accompanied by increased expression of NIS (Kogai et al., 1997). Thus, nutritional deficiency in iodine induces the thyroid NIS system to be upregulated, increasing the population of NIS on the surface of the follicular cells. The time required for changes in T3, T4, and TSH in response to nutritional deficiency in iodine vary within species and nutritional states but it is known that changes in concentration of the NIS occur rapidly (within hours) in response to changes in the level of TSH (Eng et al.,1999; Yu et al., 2002). It is now understood that this upregulation occurs as a response to iodine deficiency, perhaps even in the absence of increases in TSH (Johnston et al., 2005). Moreover, during pregnancy, upregulation occurs both by rises in thyroid-stimulating hormone (TSH) and in response to higher titers of the hormone human chorionic gonadotropin (Glinoer, 1997). It is proposed that changes in NIS populations occur rapidly (within hours) and that this is the salient mechanism for control of iodine concentrations in the thyroid (Eng et al., 1999).

Analyses of the results of this study indicate that a second effect of this upregulation is that the NIS system becomes much more refractory to inhibition of iodide uptake by perchlorate ion. [...I]n order to restrict normal transport of iodide, a greater fraction of a larger population of NIS would need to be blocked, and this would require a higher concentration of perchlorate."

Yu et al. (2002) identified similar NIS upregulation that compensated for 0.1 to 3 mg/kg-day perchlorate in euthyroid rats; the highest dose of 10 mg/kg-day was reported to overwhelm the NIS upregulation in euthyroid rats, leading to reduced thyroxin levels and corresponding TSH perturbations. Yu et al. (2002) noted:

"In the present study, the up-regulated thyroid, under the influence of TSH, was able to overcome the blocking effects of perchlorate by increasing its capacity to sequester iodide and produce hormones. This is clearly a dose-dependent phenomenon, which was overwhelmed by the blocking effects of high serum levels of perchlorate. []

A 90-day rat study of ammonium perchlorate identified reversible thyroid hormone perturbations at doses of up to 1,000 mg/kg-day without effects on thyroid weight or histopathology or any effects on sperm parameters, estrous cycle, bone marrow, or serum hormones; the highest dose of 10 mg/kg did increase thyroid weight and follicular cell hypertrophy (Siglin et al., 2000). Thus, it appears that NIS upregulation in the face of iodine deficiency increases the number of thyroidal receptors, thereby diluting impacts of low (< 100 ug/kg-day) to moderate (< 1,000 ug/kg-day) doses of perchlorate on reversible inhibition of thyroidal iodide uptake."

Consistent with the above observations in rats, long-term iodine deficiency in humans is known to rapidly induce NIS upregulation that enhances iodine uptake from the diet and leads to TSH release to maintain circulating thyroxine levels (Andersen et al., 2001). Short-term and relatively mild iodine deficiency also leads to NIS upregulation coincident with normal thyroxine levels and slightly decreased TSH release due to increased sensitivity of thyrocytes and a greater number of thyrocytes participating in thyroid function (Brabant et al., 1992). Brabant et al. (1992) administered 900 mg/day (about 13 mg/kg-day in 3 divided doses) of perchlorate for 4 weeks in healthy male subjects in order to induce a short-term, mildly iodine-deficient state, which corresponded to an estimated 25% depletion in thyroidal iodine capacity. This high exposure regimen led to nominal changes in free thyroxine and near doubling of circulating thyroglobulin, the latter which may also represent an

adaptive response to iodine deficiency providing a greater thyroxine capacity in the form of thyroglobulin in the blood (Brabant et al., 1992).

Perchlorate has been used as a pharmaceutical agent in persons with abnormally high thyroxine production such as in Grave's Disease, with sufficiently high regular dosages (e.g., 6,000 to 28,000 ug/kg-day) resulting in reduction of circulating FT3 and FT4 levels to limit the availability of thyroidal iodide via NIS inhibition. However, lower doses in humans administered orally for several days to 6 months do not appear to significantly impact circulating levels FT3 or FT4 or TSH, or to change thyroid size, despite the demonstration of reduced efficiency (percentage of radioactive iodine uptake) of thyroidal iodide uptake (Lawrence et al, 2000, 2001; Greer et al., 2002; Braverman et al., 2006; Braverman, 2009). Also, studies of occupational and environmental perchlorate exposures have failed to reveal any significant impact on thyroid function at doses that in some cases greatly exceed the currently proposed reference dose of 0.7 ug/kg-day by more than 100-fold (Amitai et al., 2007; Tellez et al., 2005; Gibbs et al., 1998; Li et al., 2000a,b, 2001; Lamm et al., 1999; Braverman et al., 2005, 2006; Braverman, 2009; Gibbs and Landingham, 2008; Kelsh et al., 2003; Huffier et al., 2006; Chang et al. 2003; Crump et al., 2000; Gibbs et al., 2004; Leung et al., 2009; Pearce et al., 2007a,b).

With respect to sensitivity of the neonate life stage, Ginsberg et al. (2007) have argued that a combination of factors may put infants at greater risk, particularly during lactation. Because the breast is one of the extrathyroidal tissues known to express NIS, these researchers expressed the concern for potential adverse effects on neonatal growth and development due to the combination of possible iodine deficiency and possible accumulation of perchlorate (and depletion of iodide) in breast milk. Kirk et al. (2005) reported on iodide and perchlorate levels in dairy and breast milk in the United States and observed a linear correlation between increasing perchlorate and decreasing iodide among 36 human breast milk samples (perchlorate concentrations ranged from 0.6 to 92.2 ug/L, mean 10.5 ug/L; iodide concentrations ranged from 4.5 to 184.5 ug/L, mean 63.3 ug/L. However, the reported high correlation ($r2 > 0.9$) was based on only six breast milk samples with perchlorate levels over 10 ug/L (Kirk et al., 2005). Larger studies of iodine and perchlorate levels in breast milk (Pearce et al., 2007b) and colostrum (Leung et al., 2009) in Boston- area women reported no correlation of perchlorate to iodine in the mother's milk (including colostrum) or in urine.

With respect to sensitivity of the fetus life stage, pregnant females and their offspring in the fetal and neonatal stages, if thyroid deficient, have been postulated as being vulnerable to perchlorate toxicity to the thyroid, although this has not been demonstrated to date in human populations (Braverman, 2009). The available scientific studies do not point to increased prevalence of cretinism, maternal goiter, or neonatal hypothyroidism in the general U.S. population or in small populations with perchlorate in public water supplies (Amitai et at 2007; Leung et at 2009; Li et al., 2000, 2001; Buffler et al., 2006; Crump et al 2000; Kelsh et al., 2003; Gibbs et al., 2004; Chang et al., 2003).

McLanahan et al. (2009) reported a biologically-based dose-response model of the HPT axis coupled with a physiologically-based pharmacokinetic model of perchlorate in rats and concluded that perchlorate may have two modes of action: one involving inhibition of NIS and a second involving reduced production/release of thyroxine from the thyroid. They pointed to findings of Yu et al. (2002) who noted:

"Recovery of serum thyroid hormones from the blocking effect of the 1.0 and 3.0 mg/kg-day doses of perchlorate lagged behind the TSH induced up-regulation in thyroidal uptake of 125I. A TSH-

induced "iodide sufficient" condition was evident in the thyroid; however, serum thyroid hormones were persistently low for days. The reason for this is unknown but suggests that, at high doses of perchlorate that may initially saturate the symporter, perchlorate may cause secondary effects on the thyroid beyond competitive inhibition of thyroidal uptake of iodide."

However, rats are recognized to have considerably lower iodine storage capacity in the thyroid and hence may be expected to exhibit perturbations in circulating thyroxine and TSH more readily than would be expected in humans. McLanahan et al. (2009) also pointed to earlier studies indicating perchlorate may displace iodide on certain binding proteins at very high concentrations in vitro (Okabe and Hokaze, 1993; Yamada, 1967), and to recent reports that perchlorate is probably concentrated in thyroid cells at high doses (Tran et al., 2008; Dohan et al., 2007). McLanahan et al. (2009) concluded that,

"A significant correlation of effects of ClO4- with serum thyroid hormones in humans has yet to he confirmed, so the importance of this potential mode of [mode of action] in humans is not known."

Moreover, the observed high dose effects on protein binding and on accumulation of perchlorate in the thyroid are reversible and not likely to be relevant to environmental perchlorate exposure levels in humans and are not associated with thyroid pathology at moderate dosages (e.g., 100-1,000 ug/kg-day) in normal and iodine-deficient rats based on detailed assessments (Paulus et at, 2007; Yu et al., 2002; Siglin et al., 2000).

In regards to sensitivity of different life stages to perchlorate thyrotoxicity, research is needed to examine the nature and extent of NIS upregulation in iodine deficient newborns and neonates, as well as assessment of the natural capacity of thyroidal iodine stores at birth to buffer any impacts on circulating thyroxine when iodine intake is relatively low or intermittent. It is generally known that thyroid deficiency leads to NIS upregulation (and increased thyroid volume) in pregnant and nonpregnant adults as well as in neonates, although the capacity of this protective mechanism is not well characterized in pregnant women or neonates. Consistent with the expected presence of NIS upregulation in mothers and infants, the available scientific studies do not point to increased prevalence of cretinism, maternal goiter, or neonatal hypothyroidism in the general U.S. population or in populations with higher perchlorate levels in public water supplies (Amitai et al., 2007; Leung et al., 2009; Li et al., 2000, 2001; Buffler et al., 2006; Crump et al., 2000; Kelsh et al., 2003; Gibbs et al., 2004; Chang et al., 2003).

In summary, although high doses of perchlorate 1,000 ug/kg-day) for extended time periods can cause reversible perturbations in thyroid function, such impacts have not yet been demonstrated at moderate doses (< 100 ug/kg-day) or the relatively low environmental doses (< 10 ug/kg-day) likely to be relevant to drinking water exposures. These findings, largely in human studies, suggest that the EPA-adopted reference dose of 0.7 ug/kg-day is a conservative and health- protective reference dose that incorporates a 10-fold uncertainty factor applied to the point of departure (7 ug/kg-day) to account for differences between healthy adults and the most sensitive population: fetuses of pregnant women who might have hypothyroidism or iodide deficiency.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p.

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Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28806
EPA Comment Code: 2500

Comment: Data shows that perchlorate is actively transported into mammary epithelial cells by the sodium iodide symporter (NIS), resulting in an accumulation of perchlorate in breast milk.[FN47: Dohan, O, C Portulano, C. Basquin, A Reyna- Noyra, LM Amzel, and N Carrasco. 2007. The Na+/I- symporter (NIS) mediates electroneutral active transport of the environmental pollutant perchlorate. PNAS 104(51):20250-20255.][FN48: Dasgupta, P. K., Kirk, A. B., Dyke, J. V., and Ohira, S.-I. (2008). Intake of Iodine and Perchlorate and Excretion in Human Milk. Environ. Sci. Technol. 42, 8115-8121.] These data suggest that perchlorate may not only inhibit iodide accumulation in maternal milk but also would be transferred in breast milk to the nursing infant where it would be predicted to inhibit iodide uptake in the infant's thyroid gland. The NIS also is found in the placenta and based on this new research it seems likely that perchlorate is actively transported across the placenta. Because the fetus and developing infant require adequate iodide for thyroid hormone function, any determination of a safe level of exposure to perchlorate should take into account this mode of action for perchlorate toxicity.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28807

EPA Comment Code: 2500

Comment: c. On the most appropriate data to estimate alternative HRLs

NRDC response: The CDC (2006/2007) data represent the best available data.

The derivation of a health-based standard for perchlorate should reflect the best available data, including published data collected and analyzed by the CDC and described by Blount et al (2006) and Blount et al (2007).[FN49: Blount BC, Valentin-Blasini L, Osterloh JD, Mauldin JP, Pirkle JL. Perchlorate exposure of the US Population, 2001-2002. J Expo Sci Environ Epidemiol. 2007 Jul;17(4):400-7. Epub 2006 Oct 18. Blount BC, Pirkle JL, Osterloh JD, Valentin- Blasini L, Caldwell KL. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environ Health Perspect. 2006 Dec;114(12):1865-71.] The CDC data have the following significant advantages over the Greer et al data used by EPA:

1. Although the CDC data are from a cross-sectional analysis, because the survey includes a large number of individuals, the variability represents random error, not bias, and the data are likely to be representative of chronic perchlorate exposure; 2. The number of individuals included in the CDC study are sufficient for the specific analysis of a sensitive subpopulation defined as women with low iodine intake; 3. A benchmark dose (BMD) analysis of perchlorate-related modulation of serum thyroid hormone concentrations is feasible; and 4. Perchlorate exposures, as measured by urinary perchlorate concentration, corresponding to the benchmark dose low (BMDL) can be converted to an estimated dose in mg/kg-day, that can be used as the point of departure for the derivation of both the MCL and HRL.

From Blount et al (2006) we know that the mean for total serum T4 concentrations in women is 8.27 ug/dL and the 25th percentile of perchlorate exposure (equivalent to 1.6 ppb perchlorate in urine) is associated with a 10% drop in total serum T4 in women with low iodine intake.[FN50: Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environ Health Perspect. 2006 Dec;114(12):1865-71.] Importantly, the unique physiology of pregnancy and interactions between the mother and fetus make both especially susceptible to the harmful effects of perchlorate; maternal T4 is the only source of thyroid hormone for the fetus in the first trimester.

Blount et al (2007) established that for women with low iodine intake (defined by the World Health Organization as urinary iodine < 100 ug/L),[FN51: World Health Organization (WHO). 1994. Indicators for assessing iodine deficiency disorders and their control through salt iodization. WHO/NUT/94.7. Geneva: WHO/International Council for the Control of Iodine Deficiency Disorders.] very low levels of perchlorate exposure were associated with decreased serum T4 and increased serum TSH; the CDC estimates that 36% of U.S. women have iodine intakes in this range. For iodine-sufficient women (defined as urinary iodine >= 100 ug/L), perchlorate exposure was associated with increased TSH. Increased TSH is an indicator that the body is attempting to compensate for a decrease in thyroid hormone production, and is clinically considered to be a more sensitive marker of subtle thyroid alteration than depressed levels of serum T4. When predicting changes in serum TSH with increasing perchlorate exposures, women with low iodine intake and TSH levels on the high end of the normal range (> 3.11 IU/L) appeared to be the most sensitive group. In this group, any increase in urinary perchlorate predicted an increase in TSH that was consistently more than twice the predicted increase in TSH for women with low iodine levels and

median TSH levels. For unknown reasons, perchlorate was not associated with T4 or TSH levels in men. The observed changes in serum T4 and TSH in women are consistent with our understanding of how thyroid hormones are regulated in the body, and with the mechanism of toxicity of perchlorate.

Importantly, the extremely low levels of perchlorate were associated with thyroid hormone disruptions - and the magnitude of these disruptions. The CDC researchers found that if a low iodine woman started with perchlorate exposure corresponding to 0.19 ppb in urine (the minimum level found), and then ingested enough perchlorate through food and/or drinking water to raise her urinary perchlorate level to 2.9 ppb (the median level found), her T4 levels would drop by 13%.[FN52: The drop in T4 predicted to be 1.06 ug/dL; the percentage decrease is calculated as compared to the average T4 level found in the CDC study (8.27 ug/dL).] Similarly, if her urinary perchlorate level increased to 5.2 ppb (the 75th percentile exposure), her T4 levels would drop by 16%. The maximum level of perchlorate exposure found was 100 ppb, which translated into a 29% decline in T4.

d. On the merits of the approach EPA used to derive HRLs

NRDC response: The Greer data no longer represent the best available data.

Because the dose-response relationship used to determine the RfD is derived exclusively from the Greer et al study, the HRL also is dependent on the Greer et al study to determine the maximum allowable level of drinking water contamination.

The Greer et al study [FN53: Greer MA, G Goodman, RC Pleus, and SE Greer. 2002. Health effects assessment for environmental perchlorate contamination: the dose- response for inhibition of thyroidal radioiodine uptake in humans. Environ Health Perspect 110:927-937.] reported on study results from intentional dosing of a small population (N=37) of healthy men and women, for only two weeks. That is, the study cannot represent realistic chronic exposure scenarios, and it cannot be considered representative of the U.S. population including infants and children. Moreover, the study lacked measurements of iodine status that is now known to be a critical variable. Other significant weaknesses with the Greer study included the fact that the low dose group contained only seven participants including only six women. Use of these limited data to calculate a regulatory trigger level has been widely criticized as inadequate by state scientific experts[FN54: Ginsberg G and D Rice. The NAS perchlorate review: questions remain about the perchlorate RfD. Environ Health Perspect. 2005 Sept; 113(9):1117-9. Erratum in: Environ Health Perspect. 2005 Nov; 113(11):A732.] and by EPA's own Children's Health Protection Advisory Committee,[FN55: Letter from Melanie Marty to Administrator Johnson regarding Preliminary Regulatory Determination on Perchlorate (November 3, 2008, PDF) http://yosemite.epa.gov/ochp/ochpweb.nsf/content/perchlorateletter.htm/$file/PerchlorateLetter.pdf] and no longer reflects the best available data.[FN56: EN Pearce, AM. Leung, BC Blount, HR Bazrafshan, X He, S Pino, L Valentin-Blasini, and LE Braverman, 2007. Breast milk iodine and perchlorate concentrations in lactating Boston-area women. J Clin Endocrinol Metab. 92(5):1673-7.] [FN57: Letter from Melanie Marty to Administrator Johnson regarding Preliminary Regulatory Determination on Perchlorate (November 3, 2008, PDF) http://yosemite.epa.gov/ochp/ochpweb.nsf/content/perchlorateletter.htm/$file/PerchlorateLetter.pdf] Despite these limitations, careful analysis of the Greer data reveal clear evidence of perchlorate toxicity in the low-dose group; three subjects showed no perchlorate effect, but four

subjects in the low-dose group had a measurable decrease in iodide uptake commensurate with perchlorate exposure.[FN58: For a complete analysis of the NAS review of perchlorate, see: Ginsberg G and D Rice. The NAS perchlorate review: questions remain about the perchlorate RfD. Environ Health Perspect. 2005 Sept; 113(9):1117-9. Erratum in: Environ Health Perspect. 2005 Nov; 113(11):A732.] Because the study authors relied on averaged data rather than individual data, the more sensitive individuals in the study group were obscured

The short duration of the Greer study, only 14 days, mean that the cumulative effects of longer-term exposure are not accounted for. A study in rats found greater perchlorate toxicity to the thyroid from 90-day exposure than from 14- day exposure (Springborn Laboratories 1998), suggesting that cumulative exposure may cause significant systemic injury that is not detectable in a short-term study. Although one sub-chronic (six month) human study with 13 volunteers has been promoted by industry as indicating that humans adapt to long-term exposure (Braverman et al. 2006[FN59: Braverman LE, EN Pearce, X He, S Pino, M Seeley, B Beck, B Magnani, BC Blount, and A Firek. 2006. Effects of six months of daily low-dose perchlorate exposure on thyroid function in healthy volunteers. J Clin Endocrinol Metab. Jul; 91(7):2721-4. Epub 2006 Apr 24.]) this study was unlikely to have adequate statistical power to detect an effect because it failed to consider the widely-recognized vulnerable populations, including infants, children, and women with low dietary iodide. The Blount (2006) study showed that these populations are much more vulnerable to perchlorate toxicity than the average population; women are more sensitive than men, iodine-deficient (urinary iodide below 100 ug/L) women are more sensitive than iodine-sufficient women, and iodine-deficient women with TSH levels on the high end of the normal range are even more sensitive than other iodine-deficient women.[FN60: Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environ Health Perspect. 2006 Dec;114(12):1865-71.] Other human studies suffer from the same limitations as the Greer study. For example, a study of chronically perchlorate-exposed pregnant women in Chile[FN61: Tellez RT, PM ChacÃ³n, CR Abarca, BC Blount, CB Van Landingham, KS Crump and JP Gibbs. 2005. Long-term environmental exposure to perchlorate through drinking water and thyroid function during pregnancy and the neonatal period. Thyroid 15(9):963-975.] that also failed to find an effect of perchlorate exposure had only three iodine-deficient female subjects out of 183 in total.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)

EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28831
EPA Comment Code: 2500

Comment: Iodine Deficiency and the IG Report

In addition to NAS, at least one peer reviewer, several researchers (Amitai et al., 2007, Crump et al. 2004, Braverman 2007, Tellez et al. 2006) and EPA's IG (December 2008 external review draft document, Scientific Analysis of Perchlorate) have suggested that iodine deficiency is the public health problem with respect to thyroid malfunction more so than perchlorate. Furthermore, the IG report suggests that improving the iodide nutrition level for pregnant and nursing women is the most effective way to prevent low maternal total iodide uptake.

The draft report also states that because perchlorate is only one of many chemicals that affect iodide uptake in the thyroid, EPA should have followed a cumulative risk assessment approach in its perchlorate risk assessment. EPA's only mention of the IG report in the NODA is to acknowledge that the IG Report commented that the agency's risk assessment " account for the activity of other compounds with similar actions on the thyroid." The FR then directs the reader to section III.C.2 for more information, but III C. 2 details issues raised by commenters regarding the occurrence analysis and not the risk assessment or the IG report.

AMWA recommends that the final IG report be released to the public and its recommendations considered in EPA's final regulatory determination, particularly with respect to the cumulative risk assessment and iodine deficiency.

The Science of Perchlorate

Several peer reviewers of EPA's PBPK model as well as the peer reviewers of EPA's 2008 health advisory referenced new studies that EPA failed to mention in this NODA. It is important for EPA as a scientific agency to objectively and correctly characterize the science of perchlorate in the regulatory determination, and consider the body of epidemiological data as well as other health and occurrence information, particularly because the topic of possible effects to pregnant women, infants and children is such an emotional one. Much has been written in the media about perchlorate and its effects and the public and decision makers look to the agency as well as to organizations like NAS to help interpret what the science is telling us.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA does not disagree that a total iodine inhibitor load, including naturally-occurring NIS inhibitors, should be considered. The Administrator of EPA has suggested a new approach that considers cumulative risks of chemical mixtures. At this time we have not given this option full consideration. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other

factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0415
EPA Comment ID: 28844
EPA Comment Code: 2500

Comment: In previous exposure assessments conducted by the EPA, such as arsenic, all available epidemiological data was factored into the modeling assumptions, including sensitive subpopulations. EPA has clearly omitted significant peer- reviewed studies that provide a significant weight of evidence finding that there is no adverse impact from exposure to perchlorate in drinking water in the subpopulations that are a focus of this reassessment as summarized in Table 1. This omission represents a significant deficiency that countermands the Agency's stated commitment [FN3: Memo to Employees from EPA Administrator Lisa Jackson, entitled "Scientific Integrity: Our Compass for Environmental Protection". May 9, 2009. http://www.epa.gov/Administrator/scientificmemo.html] and obligation under the SDWA to use the "best available peer reviewed science" for supporting sound and technical regulatory determinations.

Table 1. Epidemiological Studies Assessing Effect of Perchlorate Exposure on Children [see PDF docket ID EPA-HQ-OW-2009-0297-0415]

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28882
EPA Comment Code: 2500

Comment: Dohan et al. (2003) provide perhaps the most comprehensive review of the NIS regulation at the time of the NRC report. Dohan et al. reported that "up-regulation of thyroid NIS

expression and iodide uptake activity by TSH has been demonstrated not only in rats in vivo but also in the rat thyroid-derived FRTL-5 [Fisher rat thyroid cell line] cell line and in human thyroid primary cultures. TSH up-regulates iodide uptake activity by an increase in NIS transcription. They say: Both NIS mRNA and NIS protein levels decreased significantly after either 1 or 6 days of iodide administration. NIS mRNA levels were already significantly reduced at 6 hours following the injected single dose of iodide. In contrast, a significant decrease of NIS protein levels was detected only at 24 hours. After TSH withdrawal, a reduction of iodide uptake activity is observed in FRTL-5 cells. This is a reversible process, as iodide uptake activity can be restored by TSH. The NIS half-life is approximately 5 days in the presence and approximately 3 days in the absence of TSH (Dohan et al., 2003). Other studies support up- regulation of NIS during changing levels of iodine (e.g., Eng et al., 1999; Wagner et al., 2002; Merrill et al., 2003; Pedraza et al., 2006; Norden et al., 2007; and Bizhanova and Kopp, 2009).]

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28898
EPA Comment Code: 2500

Comment: At a recent symposium on perchlorate held in conjunction with the annual Society of Toxicology (SOT) meeting in Seattle, Lamm et al. (2008) presented their initial reanalysis of the NHANES dataset used by Blount et al. (2006) with an adjustment for urinary creatinine. Lamm et al. considered a subset of women from the Blount et al. (2006) study who were of childbearing age (15-44 years old; the Blount et al. (2006) study group included all women over the age of 12) as well as the interaction of thiocyanate and nitrate, both in urine. They found there was no significant association between perchlorate and total T4, including women with urinary iodide less than 92 ug/g (Figure 3).

Figure 3. Urinary reanalysis results of the NHANES data [see PDF docket ID EPA- HQ-OW-2009-0297-0662]

In a peer-reviewed letter to the editor of Thyroid, Gibbs and Van Landingham (2008) reviewed data from their previously published study (Tellez et al., 2005), and showed that in a cohort of pregnant women in Chile, the data do not support the association between environmental perchlorate

exposure and changes in thyroid hormones and are consistent with the recent negative findings by both Pearce et al. (2007a) and Lamm et al. (2008), both presented at the Seattle SOT meeting.

More recently, Mendez et al. (2009) used probabilistic modeling to estimate the total dose of perchlorate from food and drinking water using three drinking water scenarios based on UCMR1 data. The highest estimated dose through water and food was 0.15 ug/kg-d at the 95th percentile, well below the RfD of 0.7 ug/kg-d. When compared to the NHANES 2001-2002 estimates based on urinary output (used by Blount et al.), they found that intraday variability contributed to the overestimation of dose based on the NHANES data. Interestingly, they also found that the urinary excretion of perchlorate in NHANES 2003-2004 was significantly lower than in 2001-2002. Two data points do not represent a trend, but this lower urinary excretion may represent lower doses through food and water in subsequent NHANES studies.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28900
EPA Comment Code: 2500

Comment: Steinmaus et al. (2007)

Steinmaus et al. (2007) used the same dataset as Blount et al. (2006) to assess the correlation between smoking, thiocyanate and urinary perchlorate, and thyroid hormone levels. The same methodological issues reported for Blount et al. (2006) apply to this study. As in Blount et al. (2006), the authors did not find any interaction between perchlorate and smoking and TSH or total T4 in women with urinary iodine levels greater than or equal to 100 ug/L or in men. They did conclude that in women with urinary iodine less than 100 ug/L, perchlorate increased the risk of lower total T4 and higher TSH, just as was reported in the Blount et al. study. This association was stronger when the woman was also a smoker or had high urinary thiocyanate levels.

Amitai et al. (2007)

This ecological study aimed to "...assess the effect of gestational perchlorate exposure through drinking water on neonatal thyroxine (T4)" by comparing T4 levels among newborns whose

mothers lived in areas with drinking water perchlorate levels associated with "very high exposure" (10 to 100-fold greater compared to levels in the U.S.; >=340 ug/L), "high exposure" (42-94 ug/L), or "low exposure" (<3 ug/L). T4 levels were measured within 36 to 48 hours after birth but there was no comment on whether the infants were breast fed or formula fed during the postnatal period. The authors found that there were no differences between neonatal T4 levels among the groups. This study provides evidence that the current RfD and values greater are conservative and health protective to the most sensitive individuals in the population.

Pearce et al. (2007)

The objective of the Pearce et al. study was "to determine whether breast milk iodine concentrations in Boston-area women are adequate for infant nutrition, and whether breast milk iodine concentrations may be associated with environmental perchlorate or cigarette smoke exposure." Pearce et al. measured breast milk iodine and perchlorate concentrations as well as iodine, perchlorate, and cotinine in urine. They then compared the levels found in breast milk to 17 commercial infant formulae. Neither breast milk nor urinary perchlorate levels were significantly correlated with breast milk iodine concentrations. Although perchlorate was detectable in infant formulae, the levels were lower than in breast milk. A significant number of women in this study had iodine levels that were insufficient to meet the infant's needs, but the authors did not suggest this was due to perchlorate exposure or that it represents a chronic iodine deficiency.

Kirk et al. (2005)

With the aim to determine what amount of perchlorate children are exposed to, Kirk et al. measured perchlorate and iodide levels in cow and human breast milk and compared these values to corresponding levels of perchlorate in drinking water in the area. Perchlorate was measurable in 81 of the 82 samples. The average perchlorate levels in cow milk and human milk were 2 and 10.5 ug/L, respectively. The maximum levels in cow and human milk were 11 and 92 ug/L, respectively. There was no correlation between levels of perchlorate in breast milk and perchlorate in drinking water. The authors speculated that there was a correlation between higher levels of perchlorate and lower levels of iodine in breast milk; however, they note that this relationship only existed for the breast milk samples with the highest perchlorate levels (6 subjects out of 82). The authors recognize that this relationship may be coincidental due to the small number of samples with perchlorate levels greater than 10 ug/L, stating that "If we take all the available data, there is no meaningful correlation between the perchlorate and iodide levels in breast milk." As with previous studies, due to the design, this study was not able to evaluate a causal relationship.

Kirk et al. (2007)

To determine the variability in the excretion of perchlorate, thiocyanate, and iodide in human milk, Kirk et al. had lactating women collect six samples of milk on each of three days or as many samples as possible over three days. They found that a significant variation over time for all the anions tested. The average iodide, perchlorate and thiocyanate levels were 87.9 ug/L, 5.8 ug/L, and 35.6 ug/L, respectively. The study was not designed to determine whether perchlorate or thiocyanate contributed to IUI in mammary tissue. This study was a biomonitoring study and did not measure any adverse effects or exposures.

Dasgupta et al. (2008)

"The objective of this present study was to study the excretion of perchlorate, thiocyanate, and iodine in milk and urine and relate the observed pattern within the broad framework of parallel/competitive transport by the NIS." Using breast milk and urine samples from 13 lactating women and using EPA default values for infant body weights and milk intakes, the authors mathematically modeled infant intakes and doses of iodide, perchlorate, and thiocyanate. They calculated the fraction of iodide, perchlorate, and thiocyanate in breast milk compared to the total that is excreted in both breast milk and urine. They used a ratio of these fractions in milk to determine the selectivity of either perchlorate or thiocyanate over iodide. They report "that 12 of 13 infants did not have an adequate intake of iodine...and 9 out of 13 infants were likely ingesting perchlorate at a level exceeding the reference dose..." They also concluded that the selectivity of perchlorate over iodide was 3.14+/-1.2.

There are a number of unresolved issues related to the experimental design of this paper. The population is small and there is no information on the selection process of the participants (i.e., they are not a random sample). Only three biological variables were measured in the women. The rest of the variables, including the variables used to derive the conclusions, are calculated from these three or are default values for infant intake and infant weights. The three measurements were the concentrations of perchlorate, iodine, and thiocyanate in urine and breast milk. Where other research has measured more biologically relevant information, such as serum concentrations of analytes that would be most reflective of relative concentrations at the NIS (Tonacchera et al., 2004; Pearce et al., 2007), this work is based on very few measured observations. The estimated doses, the key variable for understanding possible effects, are based on average body weight and intakes for an infant. For such a simple and critical variable and in such a small study population, it is surprising that actual body weights were not measured.

In addition to study design, the data presented in this paper appear to contradict the interpretation by the authors of the paper. Based on estimated weights, the authors say that nine out of 13 infants are consuming daily doses in excess of the RfD, yet Table 1 of Dasgupta et al. suggests there are 8 infants who exceed the RfD of 0.7 ug/kg-d (subjects 1, 2, 8, 11, 13, 15, 16, 20). Furthermore, if one reviews these estimates to measured variables, the infants with estimated perchlorate doses greater than the RfD are also estimated to have the greatest iodine intake. By plotting the values for total iodide excretion (column 4), total perchlorate excretion (column 7), estimated maternal breast milk iodide excretion (equivalent to estimated infant iodide intake; column 5), and estimated maternal breast milk perchlorate excretion (product of total perchlorate excreted and percent of perchlorate in milk; column 7 x column 9) found in Table 1 of the paper, the results demonstrate that perchlorate and iodide are positively correlated (See Figure 4). If perchlorate was inhibiting the transport of iodide into milk, the association would be negative.

Figure 4. Plotting of data reported by Dasgupta et al., 2008 to illustrate the association between concentrations of iodine and perchlorate in urine and milk in lactating women. [see PDF docket ID EPA-HQ-OW-2009-0297-0662]

In addition to the questions regarding interpretation of the data presented in this paper, there are concerns about the interpretation of their previous work (Kirk et al., 2005) and how that study impacts this recent study. For example, Dasgupta et al. (2008) remark that "in real mothers perchlorate does inhibit the transport of iodine into milk and because of competitive inhibition both analytes cannot be high at the same time." This statement, however, is based on a previous study in

which the researchers defined their cut off values[FN16: The cut off values from Kirk et al. (2005) were defined as follows: High iodide in breast milk was greater than 60 ug/L and high perchlorate in breast milk was greater than 20 ug/L.] above which milk iodide or perchlorate was considered "high." They report that no milk samples had both high perchlorate and high iodide (Kirk et al., 2005). In the present study, they report the same trend although they do not define a cut off value. Yet if the previous cut off values are applied to the current study, there are many samples that had simultaneously high perchlorate and iodide (Figure 4). Based on the previous conclusions about competitive inhibition of analytes (Kirk et al., 2005), this study does not demonstrate that perchlorate competitively inhibits iodide transport into milk at the concentrations experienced by these women.

Schier et al. (2009)

The authors measure the concentration of perchlorate in reconstituted powdered infant formula and used this information to estimate a mean and upper-bound dose of perchlorate in infants solely fed formula. They also estimated the perchlorate concentration in water that would cause an infant in the 10th, 50th or 90th percentile of body weight to receive a dose equal to the RfD every day. The authors concluded that some infants could be at risk for exceeding the RfD even with minimal amounts of perchlorate in water used for reconstitution, but "the clinical relevance of exceeding the perchlorate RfD in both an iodide-sufficient and iodide-deficient state are unclear."

This study provides information to the literature on potential exposures given that all the assumptions made about exposure hold true. This study is focused on the exclusively formula fed infant. The most sensitive subpopulation for perchlorate health effects and the group that the RfD is based, is fetuses of hypothyroid mothers. This paper compares the RfD to estimated doses in a population that is not the considered the most sensitive. The RfD is an

...estimate with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

This report does not demonstrate that this population is receiving doses of perchlorate at or above the RfD. This study suggests that some individuals have the potential to exceed the RfD, if all the assumptions implied hold true. Exceeding the RfD is not or meant to be a bright line threshold of effects. As noted above, the perchlorate RfD is based on a NOEL in addition to an UF adjustment.

McLanahan et al. (2009)

In an attempt to evaluate the mode of action of perchlorate, McLanahan et al. coupled a biologically-based dose response model of the hypothalamic-pituitary- thyroid axis with a PBPK model for perchlorate. The model was based on rats and evaluated changes in serum thyroid hormones with exposure to doses of perchlorate up to 10 mg/kg-d (a DWEL of 350,000 ppb). With this high dose, the authors found that the model outputs were inconsistent with observed data from experimental studies (Yu et al., 2002). The authors must add a numerical adjustment factor to their model so that output from the model agrees with experimental data. They conclude that:

ClO4- administered in drinking water (or by other routes of administration) interacts with the rat thyroid gland itself, potentially altering thyroid hormone synthesis or secretion. This interaction is in

addition to blocking thyroidal uptake of iodide. Current presumptions of a single MOA for ClO4- on the HPT axis do not appear tenable based on these results.

Modeling can be very valuable in research. This model, however, is based exclusively on rats. As many have noted, rat and human thyroid endocrinology must be evaluated carefully as the differences between the two species are important. Rats have smaller stores of thyroid hormones and are more sensitive to IUI than humans (NRC, 2005). This model is not able to predict output that is consistent with observed experimental data. Thus, without the addition of a numerical adjustment factor (called the "proportional inhibition term") this model does not produce comparable results to experimental data. The need for this numerical adjustment factor suggests unaccounted data needs or terms in the model, a species difference, or the effects of pendrin given the higher dose levels. The authors say no more than what is quoted above and provide no additional information as an explanation.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Danielle Blacet
Commenter Organization: Association of California Water Agencies
EPA Document ID: EPA-HQ-OW-2009-0297-0208
EPA Comment ID: 28918
EPA Comment Code: 2500

Comment: Please accept the attached comments from the Association of California Water Agencies on the perchlorate supplemental request for comments. Thank you for your consideration.

Danielle

Attachment

September 16, 2009

Water Docket Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Ave., NW. Washington, DC 20460

Re: Docket ID No. EPA-HQ-OW-2009-0297, Perchlorate Supplemental Request for Comments

To Whom It May Concern:

The Association of California Water Agencies appreciates the opportunity to comment on the United States Environmental Protection Agency's Supplemental Request for Comments on the perchlorate regulatory determination. ACWA represents over 450 public water agencies in California that collectively supply over 90% of the water delivered in California for domestic, agricultural and industrial uses. ACWA agencies are integrally involved in all aspects of surface water and groundwater management statewide to ensure that water supply needs are adequately addressed and are committed to ensuring that drinking water is safe for customers throughout California.

ACWA and its members have a long record of supporting a timely and consistent standard setting process, both at the state and federal levels, developed through regulatory channels and governed by good science. This support extends to the USEPA regulatory determination for perchlorate. In California we have worked diligently with the Office of Environmental Health Hazard Assessment (OEHHA) and the Department of Public Health (DPH) on many drinking water regulations, including the recent adoption of a maximum contaminant level of 6 parts per billion for perchlorate.

As the Environmental Protection Agency reviews its initial regulatory determination for perchlorate including the potential options for evaluating whether there is a meaningful opportunity for human health risk reduction from perchlorate through a national primary drinking water regulation, ACWA would like to offer the following comments for consideration in addition to responses for questions posed by USEPA: Â Issues for consideration: Â 1) USEPA should carefully consider important epidemiological data when reviewing their regulatory determination.

In four recent rule-making efforts by the USEPA involving arsenic, disinfection byproducts (DBPs), radon, and uranium, the risk assessments are based entirely on epidemiological data. In the case of arsenic and DBPs, they devote significant time and resources to reviewing numerous epidemiological studies with one study selected in each case to actually quantify the risk.

For example, the Federal Register Notice of the Arsenic Rule had almost three pages of discussion of the epidemiological data (7025 - 7027) including reference to epidemiological papers Lewis et al., 1999, Buchet et al., 1999; Kurttio et al., 1999, Chen et al., 1985; 1988; 1992; Wu et al., 1989, Hopenhayn- Rich et al., 1996; 1998, Smith et al., 1998, Morton et al., 1976; Valentine et al., 1992; Wong et al., 1992. In spite of several recent and well-designed studies available for review, the perchlorate regulatory determination appears to be the only instance where the epidemiological literature was not sufficiently considered.[FN1: Crump et.al., 2000, Tellez et.al., 2005, and Amitai et.al., 2007] Because USEPA routinely incorporates epidemiological data into these sorts of regulatory determinations, they should do so in this case as well.

Response: EPA acknowledges and thanks you for providing additional information related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other

factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group (EWG)
EPA Document ID: EPA-HQ-OW-2009-0297-0499
EPA Comment ID: 28935
EPA Comment Code: 2500

Comment: The most recent studies show widespread exposures:

The notice in the Federal Register concludes with a section that discusses studies published since EPA adopted the NAS RfD for perchlorate. Since EPA adopted the NAS RfD of 0.7 ug/kg/day, several comprehensive studies have been published that shed new light on the degree of perchlorate contamination in the United States and the possible health implications of this contamination. In a fact sheet that accompanied the August 19th notice in the federal register, the agency notes, "The key focus of the re-evaluation has been consideration of exposure of infants and young children." EWG fully supports this renewed focus on the health threats that perchlorate presents for infants and young children. Research from the last few years has established that not only do infants and children have higher exposures to perchlorate when compared with adults, they are also more vulnerable to its toxic effects. A comprehensive epidemiological study from the CDC also calls into question the safety of the current RfD (Blount et al 2006b). Below, we list the evidence from recent research that confirms that infants and children are particularly at risk from perchlorate contamination of drinking water and why EWG believes that a maximum contaminant level (MCL) of no higher than one ppb is a necessary public health measure:

- A major CDC bio-monitoring study found that children ages six to 11 have higher exposure to perchlorate compared with adults (Blount et al 2006a) - An FDA study that found perchlorate contamination of 74% of nearly 300 types of commonly consumed foods and beverages also confirmed that young children are exposed to more perchlorate, per unit of body weight, from contaminated food when compared with adults (Murray et al 2008) - A recent study from CDC scientists found that powdered infant formula is widely contaminated with perchlorate (Schier et al 2009) - Infants and children require more iodine on a body weight basis than adults and could therefore be more vulnerable to a thyroid toxin like perchlorate that inhibits iodine uptake by the thyroid gland (WHO 1998) - Breast milk testing in the U.S. has revealed wide-spread contamination with perchlorate (Kirk et al 2005, Kirk et al 2007, Pearce et al 2007) - Adequate levels of thyroid hormones are critical to normal brain development in infants and children and even subtle decreases in these hormones during these critical periods can have irreversible effects on cognition (Haddow et al 1999, Pop et al 1999) - A major epidemiological study from the CDC finds that perchlorate exposures far below the current RfD are associated with significant changes in thyroid hormone levels in women (Blount et al 200b)

Each of these points is further discussed in detail below:

CDC bio-monitoring study finds that children have higher perchlorate exposure: In 2006, CDC scientists published the results of a major bio-monitoring study in which nearly 3,000 Americans

ages six and older who are representative of the U.S. population were tested for perchlorate. Every single participant was found to have been exposed to perchlorate. Furthermore, children ages six to 11 had the highest exposure of any group tested, with urinary perchlorate levels that were 1.6 times higher on average than in adults (Blount et al 2006a).

As far as EWG is aware, there has been no testing of urinary levels of perchlorate in children under the age of six or infants in the United States. While this is a significant data gap, there is reason to believe that infants and young children may be among the most highly exposed groups in this country. Infants are at risk for high exposures to perchlorate due to widespread contamination of breast milk and infant formula, while young children are especially at risk due to widespread food contamination, especially of dairy products such as cow's milk. Widespread contamination of foods that infants and young children consume heavily coupled with the fact that children consume more food and water per unit of body weight than adults and their relatively small size in comparison with adults virtually guarantees that infants and young children have even higher perchlorate exposures than children in the six to 11 age group and adults.

FDA finds widespread perchlorate contamination of commonly consumed foods and beverages: In 2008, scientists from the FDA published the results of a study in which 285 commonly consumed foods and beverages were tested for perchlorate. Their results revealed widespread food contamination in the U.S.; perchlorate contaminated 74% of foods and beverages that were tested. The FDA scientists went on to estimate daily perchlorate exposures from contaminated foods and beverages (excluding tap water) and found that exposures were highest among two year olds. For this age group, perchlorate exposures from contaminated food and beverages ranged from 50 and 56% of the current EPA RfD of 0.7 ug/kg/day (Murray et al 2008).

The FDA findings are especially concerning because they show that children have high baseline exposures to perchlorate from commonly consumed foods and beverages. Overall, the FDA analysis found that children ages 10 and under are most highly exposed to perchlorate from contaminated foods and beverages. This is because children consume items from food groups that are heavily and consistently contaminated with perchlorate, especially dairy foods. In addition, their smaller size in comparison with adults means that, pound for pound, they are exposed to higher amounts of perchlorate than adults.

The FDA study, while concerning in itself, has even more profound implications for the children who live in any one of the 26 states in which perchlorate has been found in drinking water. EWG analysis finds that every proposed or final drinking water standard for perchlorate in the U.S. fails to protect two year olds from routine, daily, unsafe exposure when combined food and water exposures are considered. A two-year-old of average size could exceed EPA's current RfD by drinking water with just four ppb of perchlorate contamination (EWG 2008). A two-year-old of smaller size or with above average daily water consumption could easily exceed the RfD at even lower drinking water concentrations. The widespread food contamination by perchlorate leading to high baseline perchlorate exposures among children underscores the need to set an MCL of <1 ppb to minimize combined food and tap water exposure among children.

CDC scientists find perchlorate in infant formula: Earlier this year, CDC scientists published results of a study in which they tested 15 brands of infant formula; they found perchlorate contamination of all brands tested. The two most contaminated brands, made from cow's milk, accounted for 87% of the U.S. powdered formula market in 2000. The CDC team warned that mixing perchlorate-

tainted formula powder with tap water containing "even minimal amounts" of the chemical could result in exposures that exceed the current RfD. For example, they note that "reconstitution of PIFs (powdered infant formulas) with water containing perchlorate levels of at least 4 ug/l resulted in 26/48 (54%) dosing scenarios exceeding the RfD". In several other dosing scenarios, the formula was so heavily contaminated with perchlorate that formula consumption alone resulted in exposure levels above the RfD (Schier et al 2009). This study again underscores how easily vulnerable populations such as formula fed infants can exceed EPA's perchlorate RfD when cumulative exposures from contaminated food and tap water are considered.

Increased iodine requirements in infants, children suggest particular vulnerability to perchlorate: The World Health Organization (WHO) recommends that the average adult should consume 2 micrograms of iodine per kilogram of body weight per day to meet daily nutritional requirements. In contrast, WHO recommends that young children and infants ingest 3 and 7.5 times more iodine respectively per kilogram of body weight per day than non-pregnant adults (WHO 1998). This is because thyroid hormone production and turnover are greater in infants and children, compared with adults (Ginsberg et al 2007, Meikle 2007). High iodine requirements among infants and children may result in particular vulnerability to perchlorate related changes in thyroid hormone levels among these populations when compared with adults. This is because perchlorate interferes with iodine uptake by the thyroid gland, and since infants and children require more iodine that adults, any contaminant that disrupts this process may impact them more severely. This particular vulnerability is recognized by the National Academy of Sciences, which noted in a 2005 report that in "pregnant women, infants, and children, and people who have low iodide intake or pre-existing thyroid dysfunction, the dose [of perchlorate] required to cause a decrease in thyroid hormone production may be lower [than for non- pregnant adults]" (NAS 2005).

Studies reveal widespread perchlorate contamination of breast milk: In three recent studies from CDC and academic scientists, samples of human breast milk from different parts of the country were tested for perchlorate. Every single sample of breast milk in all three studies was positive for perchlorate (Kirk et al 2005, Kirk et al 2007, Pearce et al 2007). In addition, the average levels of perchlorate in breast milk in these studies would result in exposure above the agency's RfD for a significant numbers of breast-fed infants.

Further, in all three breast milk studies, a significant number of samples contained insufficient levels of iodine to meet the requirement of breast fed infants, meaning that not only would babies drinking this breast milk be exposed to hazardous levels of perchlorate by EPA's standards, but they would also be deficient in the iodine necessary to counteract the thyroid hormone lowering effects of the contaminant, thereby magnifying potential health effects of perchlorate in these infants.

While there is no question that perchlorate in both food and tap water contributes to breast milk contamination, minimizing perchlorate in tap water is an important overall way in which to decrease this contamination. There is presumably a relationship between the amount of perchlorate a woman consumes and the perchlorate concentration in her breast milk; decreasing her exposure by minimizing tap water contamination would most likely result in decreased perchlorate levels in her breast milk. In addition, those infants who are fed both breast milk and powdered formula have multiple sources of exposure from contaminated breast milk, formula, and tap water used to reconstitute the formula. For all of these reasons, setting an MCL for perchlorate of <1 ppb would present a meaningful opportunity to reduce breast milk contamination and decrease perchlorate exposure among infants.

Infants and children particularly vulnerable to toxic effects of perchlorate: Adequate circulating levels of thyroid hormones are critical to maintaining normal metabolism in adults, but are especially important for infants and children. Infancy and early childhood are times of rapid growth and brain development, and any abnormal decreases in thyroid hormone levels during these critical periods may lead to inhibition of these processes. Infants and children may suffer from stunted growth and delays in intellectual development if they have inadequate levels of thyroid hormones. These impacts on growth and brain development can be long-term and irreversible. These concerns recently prompted Dr. Melanie Marty, Chair of EPA's Children's Health Protection Advisory Committee (CHPAC) to state in a November 3rd, 2008 letter to the agency:

"The life-long consequences of impaired brain development are sufficient to merit setting a protective MCL for perchlorate (CHPAC 2008)."

Perchlorate exposures below RfD affect thyroid hormone levels: Lastly, EWG would like to address the agency's current RfD for perchlorate. On the last page of the notice, the agency states, "EPA agrees that additional important data have become available since the RfD was derived in 2005. However, EPA has evaluated the new data and has decided to make the regulatory determination based on the current RfD." EWG strongly disagrees with this finding and we urge EPA to revise the RfD to reflect the most current science. The current RfD was derived from the Greer study, which has been critiqued in the peer-reviewed literature and by a state regulatory agency, the Massachusetts Department of Environmental Protection.

A recent large-scale epidemiological study from CDC calls into question the actual safety of the agency's RfD (Blount et al 2006b). In September of 2006, CDC scientists published the first major epidemiological study using National Health and Nutrition Examination Survey (NHANES) data on the potential health impacts of chronic perchlorate exposure. Researchers found a statistically significant, dose-dependent association between perchlorate exposure and changes in thyroid hormone levels in all of the women in the study. In women with lower iodine levels (one third of American women), perchlorate exposure far below the EPA RfD was associated with significant changes in thyroid hormone levels. This is the first study to establish iodine insufficiency among women as a risk factor for perchlorate induced thyroid toxicity. This new discovery highlights a major deficiency in the Greer study; the iodine status of the 37 participants in that study is unknown.

In the Blount study, women were classified based on urinary iodine levels; those women with urinary iodine levels <100 ug/L had significant changes in both TSH and T4 associated with perchlorate exposures far below the current RfD. For a subset of women in the study with lower iodine levels [those with higher baseline thyroid stimulating hormone (TSH) values], exposure to perchlorate as low as five ppb in drinking water was associated with increases in TSH that fall into the range of a medical condition called subclinical hypothyroidism. While there is disagreement about whether this condition should be treated in non- pregnant women, there is consensus in the medical community that pregnant women who develop this condition should be treated with thyroid hormone in order to ensure normal brain development of their fetus.

The results of the Blount study call into question the safety of the RfD and raise the possibility that perchlorate exposures in infants and children may be exerting a far more significant clinical effect that previously believed. As mentioned above, infants and young children are routinely exposed to perchlorate concentrations close to the current RfD from formula, breast milk, and food exposure.

Even minimal drinking water contamination can lead to cumulative exposures that exceed the RfD among these vulnerable populations. The results from CDC's study, which did not include children under the age of 12, suggest that perchlorate exposures far below the current RfD may significantly affect thyroid hormone levels in adult women. If the results from the CDC study are extrapolated to vulnerable populations, millions of infants and children may be experiencing perchlorate-induced disruption in thyroid hormone levels during critical stages of brain development and growth at current levels of exposure, far below the current RfD.

Response: EPA acknowledges and thanks you for providing additional data related to perchlorate. EPA will continue to evaluate the available science related to perchlorate. On August 19, 2009, EPA published a Federal Register notice requesting supplemental public comments on its preliminary determination not to regulate perchlorate in drinking water (Federal Register Vol. 74, No. 159, p. 41883). In this August 19, 2009 Federal Register notice, EPA requested comments on additional interpretation of data on the level of human health concern, perchlorate frequency of occurrence in drinking water, and the opportunity for health risk reduction through a national primary drinking water standard, to help determine if it should be regulated. EPA considers both the extent of national occurrence and the severity of health effects for a contaminant, as well as other factors (e.g., sources of exposure), when deciding whether regulation presents a meaningful opportunity for health risk reduction. Therefore, the Agency considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate will be regulated.

EPA Comment Code: 2600 Comments on expanding scope of risk assessment to include other goitrogens and/or dietary iodide deficiency

Individual Comments
Commenter Name: Jonathan Borak
Commenter Organization: Yale School of Medicine
EPA Document ID: EPA-HQ-OW-2009-0297-0209
EPA Comment ID: 28508
EPA Comment Code: 2600

Comment: 3). OIG presented a compelling argument that perchlorate regulation should not be based on risk assessment of perchlorate alone, but on an assessment of the complex mixture of naturally-occurring NIS stressors that includes perchlorate. Moreover, "lack of iodine in the diet (a.k.a. iodide deficiency)" is the most important of those NIS stressors (13).

Response: See response to comment ID 28529 under comment code 2500.

Commenter Name: Andria Ventura
Commenter Organization: Clean Water Action et al.
EPA Document ID: EPA-HQ-OW-2009-0297-0528
EPA Comment ID: 28514
EPA Comment Code: 2600

Comment: EPA must also consider other exposure pathways and additional contaminants in the environment that impact thyroid function when establishing the MCL. Studies of perchlorate levels in food, including breast milk, show that the population is exposed through multiple pathways in addition to contaminated drinking water. EPA should determine potential aggregate exposures based on a broad range of contamination levels, and not just the mean, which was the basis for current estimates.

While data have also demonstrated a particular threat to the significant number of individuals, especially women of child-bearing age who are iodide deficient, the current modeling does not include this threat. Given this widespread problem (CDC estimates up to 30% of women do not get sufficient dietary iodide), it is critical to take into consideration the potential for exposure to other thyroid- active agents. Consequently, EPA must consider the cumulative impact of perchlorate, other substances in the environment that inhibit the uptake of iodide by the thyroid, and inadequate supplies of iodide in American diets, all of which makes a stringent drinking water standard necessary to be truly health protective.

Response: See response to comment ID 28529 under comment code 2500.

Commenter Name: Shannon Cunniff
Commenter Organization: Department of Defense (DOD)
EPA Document ID: EPA-HQ-OW-2009-0297-0411
EPA Comment ID: 28522
EPA Comment Code: 2600

Comment: Comment No. 10

Section III.A. 4. Request for Comment on Alternative Approaches.

Page & Paragraph Page 41886

Comment We believe that at this time, PBPK modeling is necessary to be able to more fully consider sensitive subpopulations' exposure to chemicals that bind to the NIS receptor such as perchlorate, thiocyanate, and nitrate from dietary sources and the significance of low levels of perchlorate in drinking water. EPA should consider whether thiocyanate and nitrate may have a much greater impact than perchlorate for the most sensitive subpopulations with insufficient iodide and how best this can be resolved.

Consideration should also be given to the differences in the rate of excretion of thiocyanate and nitrate in human urine compared to perchlorate and the half- life of each (relative amount of time in the body from ingestion prior to excretion and the differences in the strength of iodide uptake inhibition).

Suggested Action, Revision and References (if necessary) We also recommend validation and/or comparison of the results of the current EPA revised PBPK model (2009) with biological fluid data derived that are available from perchlorate exposure studies. Studies include those recently published by the CDC and NIEHS (Blount et al., 2009) and the longitudinal epidemiologic study of pregnant women in Northern Chile (references provided below) as well as other scientifically sound human data. The CDC and NIEHS study reported not only new sensitive subpopulation-related perchlorate and iodide biological fluid data but they also compared thiocyanate and nitrate found in maternal and fetal compartments to levels found in other published studies. We believe that consideration of such data is consistent with EPA's statement made in the FR announcement that they will "...continue to evaluate any new perchlorate data to determine its relevance to the regulatory determination in accordance with the SDWA."

References: Blount et al. 2009, "Perinatal Exposure to Perchlorate, Thiocyanate, and Nitrate in New Jersey Mothers and Newborns." Environ. Sci. Technol.
http://pubs.acs.org/doi/pdfplus/10.1021/es9008486

Tellez et al. "Long-term environmental exposure to perchlorate through drinking water and thyroid function during pregnancy and the neonatal period." Thyroid 2005, 15, 963-975.

Category* S. M.

Response: See response to comment ID 28529 under comment code 2500. EPA concluded that the PBPK modeling analysis, in the context of the perchlorate regulatory determination, is useful in examining which life stages are most susceptible to the effects of perchlorate. For example, the model indicates that a fetus may be seven times more sensitive to the effects of perchlorate than a pregnant woman. The model also allows for the estimation of the concentration of perchlorate in breast milk (thus breast-fed infant exposure) at various maternal perchlorate exposure levels. However, because of the stated limitations, EPA has decided the model does not directly bear on the current decision regarding the need for a NPDWR for perchlorate.

Commenter Name: John P Gibbs
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0636
EPA Comment ID: 28552
EPA Comment Code: 2600

Comment: 3) OTHER NIS INHIBITORS

Although the NAS committee members were aware of the significance of other NIS inhibitors and had access to the Tonaccera et al 2004 study, they were restricted by their charge to considering only perchlorate. All NIS inhibitors share the same mechanism of toxicity as perchlorate by blocking the uptake of iodide by the thyroid. The risk to public health is from the combined amount of NIS inhibition acting on the body from all three NIS inhibitors (thiocyanate, nitrate, and perchlorate). The combined total NIS inhibition load acting on the thyroid (not just perchlorate exposure) determines the total iodine uptake level and the subsequent potential for an adverse outcome. Adverse thyroidal effects of high concentrations of thiocyanate have been reported in numerous studies (Gibbs, 2006)

As noted in the OIG draft report, perchlorate, thiocyanate, nitrate and low iodine intake fit the criteria of a cumulative risk assessment. OIG reports that thiocyanate, nitrate, and iodine are found naturally in food and water sources, assuming that people are not exposed to any one of these chemicals alone, but in combination. Thus, the focus on one chemical does not in fact provide a scientifically accurate assessment of possible human health risk. The cumulative risk assessment approach provides the best opportunity to impact public health.

Response: See response to comment ID 28529 under comment code 2500.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0653
EPA Comment ID: 28560
EPA Comment Code: 2600

Comment: The 15 ppb drinking water level proposed under the October 2008 preliminary guidance is sufficiently protective as few drinking water systems were shown to exceed this level in the 2000-2001 sampling of water systems. Fewer systems are likely to even reach this level as states such as California and Massachusetts have since set more stringent drinking water levels of 6 ppb or below, and sources of potential contamination are being remediated. For these reasons, EPA has difficulty justifying that meaningful public health protection will result from regulation as the percentage of the public residing outside of states where regulations are already in place, and where perchlorate occurrence in drinking water supplies is at a meaningful level, is remarkably small. It appears that EPA has attempted to push the limit lower in an attempt to justify larger numbers of population affected in order to meet the SDWA criteria concerning exposure/occurrence. The Agency has not addressed in its analysis that the population of an area that may be impacted fails to differentiate that most adults and older children are not as sensitive to the effects of perchlorate as the fetus of a pregnant woman, the subpopulation identified by the NRC as being the most sensitive. Instead,

EPA has attempted to use the total number of population exposed by a water provider with perchlorate occurring in drinking water as being equally exposed and equally at risk. This assessment ignores that more targeted means of addressing potential sensitivities, or personal concerns, may be effected through the consumption of bottled water (a common practice that is not factored into EPA's analysis), or the provision of a diet with sufficient iodine to make a drinking water consumer less likely to be iodine deficient. Even with regulation, EPA's efforts do nothing to focus public health efforts on attaining iodine sufficiency and, therefore, miss the real public health threat.

Response: EPA disagrees. EPA is using a data driven approach considering the totality of the best available, peer reviewed data to develop an NPDWR that is protective of human health. EPA will consider the economic impacts of the proposed MCL in developing theNPDWR.

Commenter Name: Richard M. Peekema
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0419
EPA Comment ID: 28687
EPA Comment Code: 2600

Comment: I believe the percentage of iodide deficient women several decades ago was possibly half what it is at the present. It seems likely that the media coverage of excess salt intake has caused many individuals to self medicate, avoid salt, and indirectly limit their iodide intake. This changes the size of the population at risk. Similar changes are possible in the amounts of thiocyanate and nitrate which people ingest. The EPA provides the following info on p.41892 in its FR solicitation for comments:

An additional key scientific issue was raised by EPA's OIG in the report released for public comment "OIG Scientific Analysis of Perchlorate (External Review Draft)" (EPA, 2008g). The report states,

The OIG [Office of Inspector General] Analysis concludes that a single chemical risk assessment of perchlorate is not sufficient to assess and characterize the combined human health risk from all four NIS stressors, (i.e., thiocyanate, nitrate, perchlorate and lack of iodide) and that * * * Only a cumulative risk assessment can fully characterize the nature and sources of risk affecting this public health issue. Furthermore, a cumulative risk assessment allows an informed environmental decision to be made on how to mitigate the risk effectively.

The report goes on to say, Potentially lowering the perchlorate drinking water limit from 24.5 ppb to 6 ppb does not provide a meaningful opportunity to lower the public's risk. By contrast, addressing moderate and mild iodide deficiency occurring in about 29% of the U.S. pregnant and nursing population appears to be the most effective approach of increasing TIU [total iodide uptake] to healthy levels during pregnancy and nursing, thereby reducing the frequency and severity of permanent mental deficits in children.

I concur completely, and endorse this position. Additionally, the fact that iodide deficiency, thiocyanate, and nitrate content in the population at risk are all changing quantities over time make it inappropriate to set a hard and fast MCL that is scientifically sound. There is nothing wrong with changing an MCL when new information comes to light regarding the action of that contaminant on

the population at risk. It is another matter, however, when the population at risk changes over time and should in prudence be mitigating that risk by other health means.

Response: EPA has determined that a NPDWR for perchlorate is warranted. See response to comment ID 28529 under comment code 2500

Commenter Name: Kay Brothers
Commenter Organization: Southern Nevada Water Authority
EPA Document ID: EPA-HQ-OW-2009-0297-0667
EPA Comment ID: 28696
EPA Comment Code: 2600

Comment: The Safe Drinking Water Act (SDWA) specifically mandates that the EPA use the "best available peer reviewed science" for supporting sound and technical regulatory determinations. However, to date the EPA seemingly has not considered the valuable epidemiological data available in peer-reviewed literature. The epidemiological studies and other human studies, most notably Greer 2002 (Greer, Goodman et al. 2002), take into account the relative source contribution (RSC). By utilizing the wealth of data provided in these studies, the EPA would no longer need to consider Relative Source Contribution (RSC) when health effects, or no observed adverse effects levels (NOAELs), are calculated using these and other human-exposure studies. While a potential criticism lies in the theoretical absence of specific subjects with iodine deficiencies, we agree with the EPA's Inspector General in stating that regulatory action under the SDWA is not the appropriate or effective way to address the overarching public health issue - iodide deficiency. For these reasons alone, we believe that epidemiological data available for exposure to perchlorate through drinking water should be evaluated before turning to the more nebulous PBPK modeling.

Response: See response to comment ID 28718 under comment code 2600
EPA concluded that the PBPK modeling analysis, in the context of the perchlorate regulatory determination, is useful in examining which life stages are most susceptible to the effects of perchlorate. For example, the model indicates that a fetus may be seven times more sensitive to the effects of perchlorate than a pregnant woman. The model also allows for the estimation of the concentration of perchlorate in breast milk (thus breast-fed infant exposure) at various maternal perchlorate exposure levels. However, because of the stated limitations, EPA has decided the model does not directly bear on the current decision regarding the need for a NPDWR for perchlorate

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Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0647
EPA Comment ID: 28715
EPA Comment Code: 2600

Comment: Water Docket ID No, EPA - HQ - OW - 2009 - 0297

Supplemental comments regarding the fundamentally different outcomes between Greer, et al, 2002 and the Blount, et al, 2006 studies on low dose effects of perchlorate

By: Herwig Opdebeeck, SM, Opdebeeck Consulting[FN1: Mr. Opdebeeck can be reached at +41 79 658 7979, or h.opdebeeck@opdebeeck.ch.], October 8th, 2009

Executive summary

In the Blount study, an association between perchlorate levels and TSH was found at levels four orders of magnitude lower than has been found in previous studies. However, this result does not appear to represent a causal relationship between perchlorate and TSH, due to the inconsistent results exhibited by perchlorate and the other goitrogens, thiocyanate and nitrate, within the same study. To our knowledge, no in depth study has been published which explains these inconsistencies exhibited by the Blount study in a manner that would continue to support its conclusions and allow the study to be used as the basis for regulation of perchlorate. Instead, our analysis of the other substances not controlled for in this cross sectional study supports the conclusion that the inconsistent and unexpected results of the Blount study are the result of causal associations between these other substances and thyroid hormone levels.

Even though only a few of the many substances with the capability of affecting thyroid function were surveyed in the same NHANES database on which the Blount study was based, we found several that showed the same association with TSH. Added to the fact that the association of those substances with thyroid hormone was at levels that are known to cause those effects and not at levels four orders of magnitude lower as was the case for the perchlorate association, it is apparent that the association with thyroid hormone found in the Blount study is not due to perchlorate but due to a pool of goitrogenic substances of which the perchlorate background is only a marker.

In conclusion, not only didn't the Blount study show an upstream iodine inhibition (i.e., it didn't show a relationship between iodine and THs), but additionally perchlorate, which only represents 1% of the NIS goitrogen load, and all three NIS goitrogens seem to have been fully compensated by iodine - explaining the non-relationship of iodine with TH. For the NIS goitrogen perchlorate, it should also be noted that at background levels, it is a strong predictor of environmental iodine background levels. Additionally, goitrogenic compounds shown to have a direct effect on TH levels and at levels know to cause such effects, were found to be associated with TSH as well, without exhibiting the inconsistencies found in the Blount study. Finally, a plausible link can be found between those compounds and perchlorate, a marker for the goitrogenic pool through the chlorine link.

Acronyms BW: Body weight of an adult (70Kg) DW: Drinking water DWL: Daily drinking water consumption in litres (2 L) DBP: Disinfection by-products EGP: Environmental goitrogenic pool (see GC) MCL: Maximum contaminant level NAS: National Academy of Sciences =NRC NIS: Sodium iodine symporter NOEL: Non observed effect level NRC=National Research Council = NAS DWS: Drinking water standard GC: goitrogenic contaminants (substances that inhibit iodine uptake and therefore could affect TH levels or substances such as PCBs that directly affect TH levels) OIG: EPA's Office of Inspection General PHG: Public health goal RfD: Reference dose sum23PCB= the sum of the concentrations of 23 PCBs in the NHANES 2001-2002 dataset. TGL: Total (NIS) goitrogen load TH: thyroid hormone UF: Uncertainty factor UPEC (or UTGL): Urinary perchlorate equivalent concentration expressed in PEC: [Perchlorate] + [nitrate/150] + [thiocyanate/8.8] with concentrations in weight.

Response: EPA will consider the totality of the best available, peer reviewed science in developing the NPDWR for perchlorate. Data will be evaluated using a weight of evidence approach, considering each study in the context of the entire database.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0647
EPA Comment ID: 28718
EPA Comment Code: 2600

Comment: Summary

Preliminary note: When expressing a relationship between variables in a cross- sectional study we sometimes use the term "predictor of "(term used in Blount et al. study) which has the same meaning as "associated with" or "related with".

We statistically analyzed some of the other substances contained in the same NHANES 2001-2002 data on which the Blount et al. study was based, and found similar statistically significant associations between some of those substances and TSH. We did not look for associations with T4 since, after adjusting for creatinine, the association between perchlorate and T4 disappeared for the pertinent subpopulation, women of childbearing age with insufficient levels of iodine[FN4: Lamm SH, Hollowell JG, Engel A, Chen R (2007). Perchlorate, thyroxine, and low urine iodine association not seen with low creatinine- adjusted urine iodine among women of childbearing age. Thyroid 17 (s1):S-51].

Indeed there exist many other goitrogenic substances that have a different mode of action not related to iodine uptake inhibition. The Blount study is about possible effects on THs of substances present in the population sample. Therefore, all known substances that affect TH levels, all goitrogenic contaminants (GC), should have been statistically tested and controlled for as well and not only those that act through the same mechanism as perchlorate. Since iodine levels are probably not relevant to explain the Blount TH level changes as they are not associated with TH levels in the same population sample, we should, in order to find a cause, not look with priority for goitrogens that affect NIS function (i.e. uptake of iodine) but GCs that directly affect TH levels.

EPA's current RfD for perchlorate is based on perchlorate's ability to competitively inhibit the thyroid gland's uptake of iodide. It is, therefore, surprising that EPA does not raise this issue when commenting on the Blount study, but instead limits itself to discussing nitrate and thiocyanate. If the Blount et al. study was focused on the iodine uptake inhibition effect, then this would have been justified. But it was not. Instead, it was about the downstream effect, the effect on TH. There are indeed hundreds of environmental contaminants, natural and synthetic, that directly affect thyroid hormone levels and which we can call the environmental goitrogenic pool (EGP). Many have not been studied and none were tested and controlled for in the Blount study, even though the levels of some were available in the NHANES 2001-2002 database of the same population for which the perchlorate - TH relationship was found. We found that the relationship between some of those substances i.e., (certain organo- halogens) with TH was similar with the one of perchlorate.

We found that the sum of the concentrations of 23 PCBs from the NHANES 2001-2002 database was a predictor of TSH for the same Blount total population ($p = 0.0037$). For women, we found that sum23PCB was a significant predictor of TSH ($p=0.0027$) and that there was no iodine interaction, or in other words the relationship of sum23PCB was the same for all levels of iodine, or

the PCB-TSH relationship was not influenced by the iodine level. For men sum23PCB was not a significant predictor of TSH.

For the total population sample, we also found that pp-DDE was a significant predictor of TSH (p=0.0185). For women, but not for men, pp-DDE was a significant predictor of TSH (p=0.0040) and again without iodine interaction which is coherent.

We suggest that the main link between perchlorate and those goitrogenic contaminants that directly affect TH levels is the element chlorine via chlorophenols, some of which originate in disinfection by-products (DBP) and many other processes where chlorine derivates are involved. The threshold effect level on THs of organohalogens such as PCBs and other dioxin- like mostly chlorine based organic substances has been found to be in the range of 0.1 to 10 ug /l serum depending on the substance. The levels of those substances found in NHANES 2001-2002 is in this range and, as mentioned, a relationship between some of these substances and THs was found as well. This is in stark contrast with the four orders of magnitude difference between the effect level of perchlorate on THs known from the body of the literature and the perchlorate levels that were related with THs found in the Blount study.

Opting for the broad picture and looking for the most likely cause of these effects produced leads which, when compared to the data, points toward a vast pool of goitrogenic compounds, natural and synthetic as the source of impacts to TH. Of these, the low level perchlorate background is only a marker, most probably through the chlorine link, rather than the cause.

In order to answer the question presented in the heading, we propose the following steps:

2.1. Opting for the broad picture

We hear a lot about the value of holistic approaches and cumulative risk assessment in documents such as: US Environmental Protection Agency (US EPA), Framework for Cumulative Risk Assessment, EPA/630/P-02/001F, National Center for Environmental Assessment, Office of Research and Development, Washington, DC, 2003a, available at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=54944.

This is an excellent opportunity to put it in practice. EPA's OIG in its December, 2008 study on perchlorate[FN5: Office of Inspector General Scientific Analysis of Perchlorate ,Assignment No. 2008-0010, December 30, 2008.] certainly took an important step in that direction, and we agree that a cumulative approach is critical to the accurate evaluation of perchlorate's risks, and should be the underpinning for any regulatory decision making regarding perchlorate.

2.2. Looking for the "culprit(s)" where they are most likely to be

There exist many other goitrogenic substances which lead to TH level change, that have a different mode of action (not related to iodine uptake inhibition) than the traditional NIS affecting goitrogens. The Blount study is about possible effects on THs of background contaminants. Therefore, all known contaminants that affect TH levels should have been statistically tested and controlled for as well and not only those that act through the same mechanism as perchlorate. Since background iodine levels are probably not relevant to explain the Blount TH level changes, as they are not related to TH levels in the same population sample[FN6: 1. Charnley G, Perchlorate:

Overview of Risks and Regulation. Food and Chemical Toxicology, 2008. 2. Soldin OP, Tractenberg RE, Pezzullo JC. Do thyroxine and thyroid-stimulating hormone levels reflect urinary iodine concentrations? Therapeutic Drug Monitoring. 2005, 27: 178-185.], we should not look primarily at goitrogens that affect the uptake of iodine (and therefore have only a potentially indirect effect on TH levels) but goitrogenic contaminants (GCs) that directly affect TH levels.

EPA's current RfD for perchlorate is based on perchlorate's ability to competitively inhibit the thyroid gland's uptake of iodide. Therefore, it is surprising that EPA does not raise this issue when commenting on the Blount study, but limits itself to mentioning nitrate and thiocyanate. If the Blount study had been about iodine uptake inhibition effect then this would have been justified. But it was not. Instead, it was about the downstream effect - i.e., the effect on TH levels. However, in the Blount study it was assumed that iodine uptake inhibition was the upstream effect, so much so that the study population had been split into 2 groups -- iodine deficient and iodine sufficient. This only created additional inconsistencies, as it exposed additional "unexpected" relationships which should have been seen as a warning that something was amiss.

Limiting the whole issue to iodine uptake inhibitors, of course, made the study much simpler to manage, but was not the right way to draw plausible conclusions about cause.

2.3. Looking for a lead

We quote from the January 2008 Thyroid journal:

"Toxicological models and limited epidemiological studies have indicated that many organohalogen aromatic compounds, including dioxins, polychlorinated biphenyls (PCBs), and polybrominated diphenyl ethers (PBDEs), may be classified as "endocrine disruptors, as they have the potential to alter normal thyroid function."

"Because environmental exposures rarely occur singly, it is often difficult to disentangle a single exposure from other co-occurring environmental exposures and conditions that may confer risks upon children. Therefore, there is often the potential for confounding, in which both the exposure and the outcome under investigation are related to a third factor that may distort the observed exposure-disease relationship."

"In epidemiologic studies, it is critically important to identify, measure, and control for such confounders."

Therefore, other substances could have caused the TH changes.

While NHANES 2001-2002 TH levels, as mentioned before, do not reflect urinary iodine concentrations, serum PCBs, p,p'-DDE and HCB background levels predict TH levels[FN7: John D. Meeker, Larisa Altshul, Russ Hauser. Serum PCBs, p,p'-DDE and HCB predict Thyroid Hormone Levels in Men. Environ Res. 2007 June; 104(2): 296-304.] and some do so in NHANES 1999-2002 survey population as well[FN8: Mary E. Turyk, Henry A. Anderson, Victoria W. Persky. Relationships of Thyroid Hormones with Polychlorinated Biphenyls, Dioxins, Furans, and DDE in Adults. Environmental Health Perspectives. August 2007,Volume 115, Number 8.]. However the background levels of only few such substances have been measured and tested against TH levels.

Yet in the NHANES 2001-2002 survey, a few of those substances have indeed been measured and therefore can be tested for associations with other contaminants in the same survey.

2.4. Focusing initially on those type of substances that are already in the NHANES 2001-2002 survey of the same population surveyed by Blount

Since organochlorides such as PCBs, DDE and other organochlorides that have been shown to directly affect TH levels are included in that survey, it should have been obvious that those substances should have been considered in the Blount study in the first place -- or at least controlled for before any other relationship was suggested.

2.5. Comparing the data on the different "suspects" comprised in the NHANES dataset

Preliminary note: We did not look for associations with T4 since, after adjusting for creatinine, the association between perchlorate and T4 disappeared for the pertinent subpopulation, iodine-insufficient (UI<100 ug/L) women of childbearing age (see ref. 4).

(a) Perchlorate versus TSH for the total (male plus female) population

The Blount study did not show that perchlorate was a significant predictor[FN9: In this paper we use the same term "predictor of" as used by Blount et al. which means the same as "associated with" and "related with", terms we also use in this paper.] of serum TSH. ($p>0.05$) for the total population.

(b) Sum of some PCBs versus TSH PCBs are one group out of a multitude of other substances that act on thyroid function (see details in Appendix 2).

We found that the sum of the concentrations of 23 PCBs from the NHANES 2001-2002 database was a predictor of TSH for the same total population ($p= 0.0037$)

(c) Perchlorate and PCBs versus TSH controlled for gender

For women (all), Blount's data indicates that perchlorate was a significant predictor of TSH (note that Blount did not publish a p value, but we found $p= 0.0153$ and $R2=0.006$) and no iodine interaction which is consistent if the predictor is not the cause.

For women < 100 ug/l UI, perchlorate was a significant predictor of TSH ($p= 0.001$).

For women > 100 ug/l UI, perchlorate was a significant predictor of TSH ($p= 0.0249$) which is inconsistent if the predictor (perchlorate) is the cause and consistent if the predictor is not the cause.

For men, Blount found that perchlorate was not a significant predictor of TSH. Further, as mentioned in our previous comment (EPA-HQ-OW-2009-0297-0227), we found that in the Blount study there was a strong relationship between iodine and perchlorate ($p<0.0001$ and $R2= 0.36$). This is an additional indication that perchlorate could not have affected TSH, in addition to the other main arguments: i) an upstream iodine inhibition was not shown; ii) there was no relationship between iodine and THs; iii) perchlorate only represents 1% of total NIS related goitrogen load and; iv) perchlorate levels seem to have been compensated by iodine. In fact, iodine levels not only seem

to fully compensate for perchlorate levels but also for the levels of the other two NIS goitrogens, nitrate and thiocyanate or conversely, low levels of iodine were compensated for by low levels of goitrogen load (see Appendix 3).

For women, we found that sum23PCB was a significant predictor of TSH (p=0.0027) and that there was no iodine interaction, or in other words the relationship of sum23PCB was the same for all levels of iodine or the PCB-TSH relationship was not influenced by the iodine level. For men sum23PCB was not a significant predictor of TSH.

(d) pp- DDE (dichlorodiphenyldichloroethylene) as a predictor for TSH In Appendix 2, we demonstrate in detail the relationship between pp-DDE, another dioxin-like organochlorinated compound found in the NHANES 2001-2002 dataset, and TSH. The associations compared with those of perchlorate are summarized as follows:

* For the total population sample, our study found that pp-DDE was a significant predictor of TSH (p=0.0185) * For women, but not for men, pp- DDE was a significant predictor of TSH (p= 0.0040). * Further we did some additional analyses and found the following additional relationships or outcomes when investigating the association between pp-DDE and TSH: 1. There was no interaction between pp-DDE and iodine and gender, which is consistent (as it is expected in the case of a non-NIS goitrogen) 2. There was no interaction between gender and iodine. 3. There was no interaction between iodine and pp-DDE, which is consistent (as it is expected in the case of a non-NIS goitrogen) 4. There was no effect of iodine on TSH (see ref. 6), which is consistent (expected : see ref. 6) 5. After correcting for pp-DDE, an increase of perchlorate was associated with an increase of TSH, only for females (p=0.0003). 6. After correcting for perchlorate, an increase of pp-DDE was associated with an increase of TSH, only for women (p=0.004).

Conclusion: Only one single goitrogenic organochlorinated substance directly affecting the level of THs is already associated with TSH at environmental background concentrations, and all other outcomes are consistent with expected results.

2.6. Looking for links between perchlorate and the members of the goitrogenous pool

To further support the absence of a causal relationship between perchlorate with TH, ideally a second relationship -- a relationship between perchlorate and those organo- halogens that directly affect TH levels -- should be found. Although it is difficult to statistically demonstrate this relationship, due to the presence of other confounding environmental GCs, the most obvious and most widely spread common link is chlorine via chlorophenols. For additional explanation, see Appendix 1.

Following a summary of Appendix 1: -DBP road 1: From bleach/Cl2/Cl-/chloramine->-> ClO3 -> ClO4- -DBP road 2 (in presence of organic (C) material): From bleach/ Cl2/Cl-/ chloramine->-> phenols ->-> organochlorides / dioxins with DBP= Disinfection by- products

Since organo-chlorinated compounds are ubiquitous, and since we find at least 1/3 of the total dietary perchlorate where we find organo-chlorinated compounds (see Appendix 1), and since many of those have been shown to affect TH levels, it is to be expected that low levels of perchlorate are associated with TH levels as found in the Blount study. This association, however, does not demonstrate causation, as Blount suggests. Given the complicated and overlapping effect of many

substances on TH levels, assigning cause to this association between perchlorate and TH levels defies logic and does not explain the inconsistencies revealed within the study itself.

Instead, perchlorate appears to be a marker, a "witness" of the presence of ubiquitous goitrogenic contamination caused by the net effect of hundreds of substances (See also section 2.8). Instead of representing the cause of the impact, perchlorate is correlated to the presence of other ubiquitous goitrogenic substances which contribute to the overall impact on TH. This alternative explanation makes logical sense, and explains the contradictions and inconsistencies regarding the other NIS goitrogens found in the Blount study.

2.7. Finally, the "alibi": background levels found compared with known effect levels

The known threshold effect level on THs of organohalogens such as PCBs and other dioxin-like substances has been found to be in the range of 0.1 to 10 ug /l serum depending on the substance[FN10: Lesa L. Aylward, Julie E. Goodman, Gail Charnley, Lorenz R. Rhomberg. A Margin-of-Exposure Approach to Assessment of Noncancer Risks of Dioxins Based on Human Exposure and Response Data. Environmental Health Perspectives. October 2008. Volume 116, Number 10.][FN11: Lawrence M. Schell, Mia V. Gallo, Melinda Denham, Julia Ravenscroft, Anthony P. DeCaprio, David O. Carpenter. Relationship of Thyroid Hormone Levels to Levels of Polychlorinated Biphenyls, Lead, p,p'- DDE, and Other Toxicants in Akwesasne Mohawk Youth. Environmental Health Perspectives. June 2008, Volume 116, Number 6.] [FN12: Johan Maervoet, Griet Vermeir, Adrian Covaci, Nicolas Van Larebeke, Gudrun Koppen, Greet Schoeters, Vera Nelen, Willy Baeyens, Paul Schepens, Maria K. Viaene. Association of Thyroid Hormone Concentrations with Levels of Organochlorine Compounds in Cord Blood of Neonates. Environmental Health Perspectives. December 2007, Volume 115, Number 12.][FN13: Jonathan Chevrier, Brenda Eskenazi, Asa Bradman, Laura Fenster, Dana B. Barr. Associations between Prenatal Exposure to Polychlorinated Biphenyls and Neonatal Thyroid-Stimulating Hormone Levels in a Mexican-American Population, Salinas Valley, California. Environmental Health Perspectives. October 2007. Volume 115, Number 10.][FN14: Mary E. Turyk, Henry A. Anderson, Victoria W. Persky. Relationships of Thyroid Hormones with Polychlorinated Biphenyls, Dioxins, Furans, and DDE in Adults. Environmental Health Perspectives. August 2007, Volume 115, Number 8][FN15: June-Soo Park, Linda Linderholm, M. Judith Charles, Maria Athanasiadou, Jan Petrik, Anton Kocan, Beata Drobna, Tomas Trnovec, Åke Bergman, Irva Hertz- Picciotto. Polychlorinated Biphenyls and Their Hydroxylated Metabolites (OH- PCBs) in Pregnant Women from Eastern Slovakia. Environmental Health Perspectives Volume. January 2007, 115, Number 1.].

The background levels of those substances found in NHANES 2001-2002 are in this range and, as mentioned, a relationship between some with THs was also found in other NHANES data based studies (see ref. 6; ref.7-11 based on other datasets, show similar levels). This is in stark contrast to the four orders of magnitude difference between the effect level of perchlorate on THs known from the body of the literature and the perchlorate levels that were related to THs found in the Blount study.

These contaminants appear to be part of a wider ubiquitous contaminant pool, natural and manmade, in which there are all kind of GCs acting with all kind of mechanisms that influence TH levels and thyroid function. Most seem to be linked, but additional study would be required to fully understand their complex relationships with one another and with TH. For more information about relationships between GCs, see Appendix 2.

Conclusion

Suggesting that a downstream effect (TH level changes) is caused by a substance (perchlorate) without controlling for other relevant substances and at the same time neglecting to check whether that same substance has a link with a known upstream effect (iodine uptake inhibition) is not the basis of sound science. On the other hand, looking for the most likely causes of an effect (rather than a results-oriented approach seeking only to demonstrate a connection between perchlorate and TH) should produce more plausible leads. When comparing the data and the circumstantial evidence, those leads point towards a vast pool of goitrogenic compounds, both natural and synthetic, of which the perchlorate background only appears to be a marker most probably through the chlorine link.

Response: See response to comment ID 28715 under comment 2600. See also response to comment IDs 28529 and 28551 under comment code 2500. EPA is aware of the occurrence of perchlorate in some sources of hypochlorite/hypochlorous acid.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0647
EPA Comment ID: 28720
EPA Comment Code: 2600

Comment: Appendix 2

The further development of the possible link perchlorate--organohalogens--TH

* Starting from an example: pp-DDE (dichlorodiphenyldichloroethylene) is a chlorinated pesticide while on the other side bromides are soil disinfectants that form organobromides which are goitrogenic substances[FN19: Johan Maervoet, Griet Vermeir, Adrian Covaci, Nicolas Van Larebeke, Gudrun Koppen, Greet Schoeters, Vera Nelen, Willy Baeyens, Paul Schepens, Maria K. Viaene. Association of Thyroid Hormone Concentrations with Levels of Organochlorine Compounds in Cord Blood of Neonates. Environmental Health Perspectives. December 2007, Volume 115, Number 12.]. So, both of those persistent organohalogens are often found together.

* Further, when bromine (a water disinfectant just as chlorine) and chlorine are involved, halogenated furanones can be produced by the reaction of naturally occurring organic matter and bromide with the disinfectant chlorine and chloramine. Research on their concentrations in drinking water is at an early stage and they are not regulated by EPA:
http://pubs.acs.org/cen/news/86/i13/8613news7.html

[Clarification: A furanone is a furan where the H is substituted with Cl, becoming polychlorinated furanones or polychlorinated dibenzofuranones. A furan is short for dibenzofuran; a chlorinated dibenzofuran is a PCB with a furan ring in the middle].

* This shows their common link with PCBs. Therefore, the halogen bromine can join the second pathway for chlorine: From bleach/Cl2/ Cl2/Cl-/chloramine, bromides ->-> furanones or phenols

->-> organohalogens /Dioxins. Thus all those persistent GCs are mostly related qualitatively and quantitatively with each other and apparently related with perchlorate.

* Associations between NHANES 2001-2002 data for pp-DDE versus TSH and perchlorate versus TSH illustrate the following: - Association between pp-DDE and TSH, total population: significant (p=0.0185) - Association between perchlorate and TSH, total population: not significant (p> 0.05). - Association between pp-DDE and TSH, women: significant (p= 0.0040) - Association between perchlorate and TSH: women < 100 ug UI, significant (p= 0.001) - Association between perchlorate and TSH: women > 100 ug UI, significant (p= 0.0249).

Conclusion: pp-DDE and other organo-halogens all seem to be related to each other and with perchlorate within the goitrogenic pool.

Further, we performed some additional analyses on pp-DDE and found the following additional relationships or outcomes when investigating the association between pp-DDE and TSH: 1. There was no interaction between pp-DDE and iodine and gender, which is consistent as it is expected in the case of a non-NIS goitrogen 2. There was no interaction between gender and iodine 3. There was no interaction between iodine and pp-DDE, which is consistent as it is expected in the case of a non-NIS goitrogen 4. There was no effect of iodine on TSH, which is consistent as it is expected (see ref. 6). 5. After correcting for pp-DDE, an increase of perchlorate was associated with an increase of TSH, only for females (p=0.0003). 6. After correcting for perchlorate, an increase of pp-DDE was associated with an increase of TSH, only for women (p=0.004).

Conclusion: The relation of those organohalogens with TSH seem to be consistent with an effect not depending on iodine levels, contrary to the perchlorate and other NIS goitrogen relations with TSH in the Blount study which are inconsistent not only with an iodine dependent effect but also show an inconsistent effect between each other.

* Some components of this goitrogenic contaminant pool have a stimulatory or agonistic effect, others an inhibitory or antagonistic effect[FN20: Cornelia Schmutzler, Inka Gotthardt, Peter J. Hofmann, Branislav Radovic, Gabor Kovacs, Luise Stemmler, Inga Nobis, Anja Bacinski, Birgit Mentrup, Petra Ambrugger, Annette Gruters, Ludwik K. Malendowicz, Julie Christoffel, Hubertus Jarry, Dana Seidlova-Wuttke, Wolfgang Wuttke, Josef Kohrle. Endocrine Disruptors and the Thyroid Gland-A Combined in Vitro and in Vivo Analysis of Potential New Biomarkers. Environmental Health Perspectives. December 2007, Volume 115, Number S-1.][FN21: http://www.ourstolenfuture.org/Basics/chemlist.htm]. Some do not have any effect at all at environmental doses. This may explain why in cross sectional studies as those based on the NHANES data base the effect of the sum of some PCBs apparently is not always greater than each individual effect as would be expected[FN22: Kevin M Crofton, Elena S Craft, Joan M Hedge, Chris Gennings, Jane E Simmons, Richard A Carchman, W Hans Carter, Jr., Michael J Devito. Thyroid-hormone-disrupting chemicals: evidence for dose-dependent additivity or synergism. Neurotoxicology Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, North Carolina, USA. Environ Health Perspect. 2005 Nov ;113 (11):1549-54 16263510 (P,S,G,E,B).] as each individual PCB on itself can be linked to other non identified and quantified goitrogens i.e. (once again) not controlled for covariates with opposite effects.

* As mentioned, there already exist 209 known congeners of PCBs alone. They vary based on the number and positions of chlorine atoms but also on their effect (strength and direction). Many have not even been studied on their goitrogenic effect. The fact that the few that were studied, here and in other studies, were found to be predictors of TSH levels is so much the more remarkable.

* Even different groups of chemicals with different mechanisms could have synergetic or antagonistic effects[FN23: Andreas Kortenkamp. Ten Years of Mixing Cocktails: A Review of Combination Effects of Endocrine-Disrupting Chemicals. Environmental Health Perspectives, December 2007, Volume 115, Number S-1.].

* Others may be linked to each other in certain environments and not in others. For example Polychlorinated Biphenyls (PCBs) and Polybrominated Diphenyl Ethers (PBDEs) --both also called polyhalogenated phenolic compounds-- may have a cumulative effect where bromine and chlorine based disinfectants are used (for example for swimming pools) and end up as DBPs (disinfection by-products) in drinking water after having gone thru the purification plant. This link could not exist in places where one of both is not used.

* Other goitrogenic phenols, such as Bisphenol A, linked itself to polyvinylchloride (PVC) such as used in waterpipes, may be linked to this chloride and halogen pool.

* On the other side completely different types of GCs, even natural ones, could be linked indirectly to the pool as well: for example organohalogen based pesticides may be present in very low amounts in soybeans but the goitrogenic effect could instead be primarily due to the isoflavones naturally present in soymilk[FN24: Daniel R. Doerge, Daniel M. Sheehan. Goitrogenic and Estrogenic Activity of Soy Isoflavones. Environmental Health Perspectives Supplements. June 2002, Volume 110, Number S3.] or the thiocyanates present in rape or broccoli or other natural goitrogens such as genistein, resveratrol, silymarin, linuron[FN25: Environmental Protection Agency, EPA/600/P-03/002F).An Inventory of Sources and Environmental Releases of Dioxin-Like Compounds in the United States for the Years 1987, 1995 and 2000. Federal Register: December 1, 2006 (Volume 71, Number 231)] Page 69564-69565] Health Perspectives Supplements. June 2002, Volume 110, Number S3.]

* Also fluorine is considered a goitrogen[FN26: Fluoride in Drinking Water: A Scientific Review of EPA's Standards (NAS, 2006) http://www.iicph.org/docs/water- reg-20060830.htmhttp:// www.pubmedcentral.nih.gov/articlerender.fcgi?artid=476957]. So, adding fluorine in salt for dental purposes could partially neutralise the effect of added iodine. Adding fluorine, another halogen, in drinking water, which is also common, would then on itself be linked to perchlorate and the organohalogen DBPs.

* Further fluorine is a major constituent of phosphate fertilizers[FN27: http://fluoridealert.org/phosphate/overview.htm#2] and is taken up by the crop so it could, just as the goitrogenic pesticides and isoflavones, be part of the goitrogenic pool as well. Also iodine itself, the fourth halogen, is used as a disinfectant.

* Other factors, even the most unexpected (birth delivery mode) may confound the effects[FN28: Julie B. Herbstman, Andreas Sjodin, Benjamin J. Apelberg, Frank R. Witter, Rolf U. Halden, Donald G. Patterson Jr., Susan R. Panny, Larry L. Needham, and Lynn R. Goldman. Birth Delivery Mode Modifies the Associations between Prenatal Polychlorinated Biphenyl (PCB) and Polybrominated

Diphenyl Ether (PBDE) and Neonatal Thyroid Hormone Levels. Environmental Health Perspectives. October 2008, Volume 116, Number 10.].

* And finally the fact that "The R2 value of 0.061 reported by Blount et al. (2006a) for the association between TSH, perchlorate, and other significant covariates for lower-iodine women indicates that perchlorate accounts for only about 1% of the variation seen for TSH in that population"(quote extracted from ref.6.1) and that therefore about 99% is related directly to goitrogenic compounds once again strongly supports the role of perchlorate as a marker only and not a cause.

Response: EPA cannot evaluate materials that have not been peer reviewed.
See response to comment ID 28715 under comment 2600.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0647
EPA Comment ID: 28721
EPA Comment Code: 2600

Comment: Appendix 3

Based on the principle of competitive uptake inhibition, it is impossible that perchlorate would have caused the TH changes found in the Blount et al, 2006 study

According to Tonacchera et al., Thyroid, 2004[FN29: Office of Inspector General Scientific Analysis of Perchlorate ,Assignment No. 2008-0010, December 30, 2008]

RAIU= 1.22 / (1.22 +PEC)

Where PEC =serum perchlorate equivalent concentration = [ClO4_] + [SCN_] / 15 + [I_] / 30 + [NO3_] / 240 = serum perchlorate + thiocyanate/15+ iodine /30 + nitrate concentration/240 and RAIU = Radioactive Iodine Uptake.

All concentrations are in umol.

The model is only valid for this specific lab trial set-up as described in Tonacchera et al., 2004 but has been generally accepted.

Assume that PEC A is a serum perchlorate equivalent concentration equal to A and PEC B is a serum perchlorate concentration equal to B.

From the above equation it follows that if PEC A is < PEC B the RAIU, which is the incremental iodine uptake, is larger for PEC A than for PEC B.

This then also means that, if there is no iodine inhibition for a certain level B of PEC in human serum, there will not be any iodine uptake inhibition for a level A of PEC in human serum either, if PEC A

(Note that PEC includes here the iodine level as iodine itself is an iodine uptake inhibitor. Indeed the more iodine present the more the uptake of the added (incremental) dose of iodine (marked here with radioactive iodine) will be inhibited and therefore the less (radioactive) iodine of the dose will be taken up).

Further, since we assume steady state (see note below), perchlorate, SCN, iodine and nitrate urinary levels are proportional to perchlorate, SCN, iodine and nitrate effective serum levels or in other words if PEC is, for example, double in serum of person B compared to PEC in serum of person A (ceteris paribus) we can assume that urinary PEC of person B will be double the urinary PEC of person A and vice-versa.

Note: We quote: "In all risk assessments on perchlorate iodine uptake inhibition "The central assumption is that the amount of perchlorate excreted per day equals the amount ingested in the bio-monitored individuals. This is true if these individuals are near or at steady state."(See: Evaluation of the U.S. EPA/OSWER Preliminary Remediation Goal for Perchlorate in Groundwater: Focus on Exposure to Nursing Infants ,Gary L. Ginsberg,1 Dale B. Hattis,2 R. Thomas Zoeller,3 and Deborah C. Rice.(ehp, Dec. 2006).

If perchlorate risk assessments are based on this assumption there is no reason why the same assumption could not be adopted here.

Also we can say that the segment of the general US population with an average of around 200 ug/l urinary iodine, which is well above the minimum WHO (World Health Organization) recommended level of 100 ug/l UI is on average not exposed to any iodine uptake inhibition and to such a level of inhibition as to cause TH (Thyroid Hormone) changes.

Hence, if using the Tonacchera RAIU equation but with urinary PEC instead, the segment of the US population with an average of 200 ug/l U iodine and with an average U PEC B has no overall iodine uptake inhibition, then we can deduct that the segment of the US population with for example an average of 30ug/l U iodine (thus iodine level B>A) but with a PEC A < PEC B and therefore a larger incremental uptake of (radioactive) iodine, does not have any iodine uptake inhibition as well.

We found that U PEC (as defined above) of the 1/8 segment of NHANES 2001-2002 female population with the average of 228 ug/l UI was higher than the U PEC of the 1/8 segment of NHANES 2001-2002 female population with the lowest average of 31ug/l UI (and also higher than that of the subsequent higher segments), See following table1: U PEC is called TGL (total (NIS) goitrogen load) here.

Table1: NHANES 2001-2002: Relationship between urinary iodine and TGL (sorted for iodine) [see PDF docket ID EPA-HQ-OW-2009-0297-0647]

Indeed, when applying the Tonacchera equation after converting molar concentrations into concentrations expressed in weight we have for women B with urinary iodine average of 228 ug/l (n=1109/8= 139) (See table 1 above, col.1):

RAIU-B i= 1.22 / (1.22 +PEC) where PEC = [ClO4-] + [SCN-] / 8.8 + [I-] / 38 + [NO3-] / 150)

= 1.22 / (1.22 + 5.9+2205/8.8+228/38+74567/150) =1.22/(1.22 +5.9+251+6+497)=1.22/(1.22+760) =1.22/761.22 =0.0016

And for women with iodine average of 31 ug/l (n=1109/8= 139) (see table 1 above, col.1).

RAIU-A = 1.22 / (1.22 +1.5+967/8.8+31/38+19293/150) = 1.22 / (1.22 +1.5+110+0.8+129) = 1.22 / 242 =0.005.

Thus RAIU-A is about 3 times larger than RAIU-B which means that the incremental iodine uptake inhibition for A women with urinary I =31 ug/l has to be less than for B women with I = 228 ug/l. This is due to the substantially higher total goitrogen load of women with the higher iodine level; see following tables 2, 3 and 4

Table 2, iodine insufficient women (<100ug/l UI): col. 9 : total goitrogen load(TGL) is about half and each of the 3 NIS goitrogens nitrate(col. 5), thiocyanate (SCN, col.7) and perchlorate (col.8) are about half of TGL for iodine sufficient women (>100ug/l UI, table 3) and for the total population (table 4)or in other words women with sufficient iodine have about double the NIS goitrogen load.[see PDF docket ID EPA-HQ-OW-2009-0297-0647]

Since, as mentioned, B women (228 ug/l UI) are not exposed to iodine uptake inhibition, A women (31 ug/l UI) should not be exposed to iodine uptake inhibition either and therefore TH levels could not be affected by the goitrogen load (of which perchlorate only represents 1%). In other words, since we can confidently assume that NIS goitrogen load does not affect iodine uptake in the NHANES 2001-2002 women with mean iodine levels of 228 ug/l urinary iodine it follows from above calculations that NIS goitrogen load, and a fortiori perchlorate load which only represents 1% of this load, does not affect iodine uptake and a fortiori TH levels in NHANES 2001-2002 women with the lowest iodine levels of only 31 ug/l. as a mean.

Conclusion

Based on the above analysis of goitrogen levels, iodine uptake and using the Tonacchera equation, it is not possible that the ability of urinary perchlorate to significantly predict TH changes in women with urinary iodine less than 100 ug/L reported by Blount et al., 2006, is directly associated with the joint goitrogen effect of nitrate, perchlorate and thiocyanate. Thus, it is not possible that the association is directly connected to perchlorate alone. More likely, the higher goitrogen load of iodine sufficient women is related to a healthier diet, one rich in vegetables and fruit.

Response: EPA cannot evaluate calculations that have not been peer reviewed.

Commenter Name: Nsedu O. Witherspoon
Commenter Organization: Children's Environmental Health Network
EPA Document ID: EPA-HQ-OW-2009-0297-0674
EPA Comment ID: 28739
EPA Comment Code: 2600

Comment: EPA must also consider other exposure pathways and additional contaminants in the environment that impact thyroid function when establishing the MCL. Studies of perchlorate levels in food, including breast milk, show that the population is exposed through multiple pathways

in addition to contaminated drinking water. EPA should determine potential aggregate exposures based on a broad range of contamination levels, and not just the mean, which was the basis for current estimates. While data have also demonstrated a particular threat to the significant number of individuals, especially women of child bearing age, who are iodide deficient, the current modeling does not include this threat.

Given this widespread problem (CDC estimates up to 30% of women do not get sufficient dietary iodide), it is critical to take into consideration the potential for exposure to other thyroid-active agents. Consequently, EPA must consider the cumulative impact of perchlorate, other substances in the environment that inhibit the uptake of iodide by the thyroid, and inadequate supplies of iodide in American diets, all of which makes a stringent drinking water standard necessary to be truly health protective.

Response: EPA will consider a variety of sources of perchlorate in developing the NPDWR.
As demonstrated in the in the August 2009 Supplemental Request For Comments, breast fed infants is a group identified by EPA as of interest.
See response to comment ID 28529 under comment code 2500.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28804
EPA Comment Code: 2600

Comment: Other contaminants are known to also interfere with iodide uptake via a similar or identical mechanism. For example, the widespread water contaminant, nitrate has a shared mechanism of action as does the chemical thiocyanate, found in cigarette smoke and in some foods.[FN44: Ginsberg G and D Rice. The NAS perchlorate review: questions remain about the perchlorate RfD. Environ Health Perspect. 2005 Sept; 113(9):1117-9. Erratum in: Environ Health Perspect. 2005 Nov; 113(11):A732.] There is some indication in the CDC data analyzed by Blount et al. that nitrate may be a factor in the modulation of thyroid hormone status. An independent analysis by OEHHA staff found an interaction between perchlorate and thiocyanate exposure and tobacco smoke exposure on thyroid hormone. It is also known that perchlorate and thiocyanate are found in breast milk.[FN45: Kirk, AB, Dyke JV, Martin, CF, Dasgupta PK. 2007. Temporal patterns in perchlorate, thiocyanate, and iodide excretion in human milk. Envrion Health Perspect.115(2):182-6.]

Response: See response to comment ID 28529 under comment code 2500.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0227
EPA Comment ID: 28817
EPA Comment Code: 2600

Comment: Water Docket ID No, EPA - HQ - OW - 2009 - 0297 : comments

Perchlorate: The Greer Non Observed Effect Level (NOEL) and the NAS Reference Dose (RfD) are significantly inaccurate and do not provide a defensible basis for regulation

By: Herwig Opdebeeck, SM, Opdebeeck Consulting

In its Perchlorate Supplemental Request for Comments, published in the Federal Register on August 19, 2009, EPA states that its preliminary regulatory determination will be based upon the RfD and risk assessment derived from the 2002 Greer study. However, as discussed below, the Greer NOEL did not take into account background effects, including the effects of other goitrogens, and is thus not a true NOEL. The true NOEL is the perchlorate dose administered in the Greer study (7 ug/kg-day), plus the dose corresponding to the background effect. The fact that this background level has not been added and is not taken into account, leads to a fundamental flaw in the perchlorate risk assessment and should not be relied upon to either regulate perchlorate or establish an RfD .

Response: EPA disagrees.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0227
EPA Comment ID: 28819
EPA Comment Code: 2600

Comment: Indeed, analyzing the NHANES database, we found that the perchlorate NOEL -- identified in the Greer study as the point at which the slightest decrease in iodine uptake occurs -- is not 7 ug /kg-day, but 157 ug /kg-day absent any perchlorate or perchlorate equivalent background level in the Greer cohort (which is assumed to be representative for the US population).

Second, and perhaps more significantly, even though the level of background perchlorate is low, other goitrogens in the environment represent a very significant perchlorate equivalent background, 22 times more potent than the Greer NOEL and more than 2,200 times more potent than the perchlorate background level itself for the general population (for women with insufficient iodine (<100 ug UI) the total goitrogen load and perchlorate background are about half, see study addendum 1. This should reflect on the goitrogen level in general and the perchlorate level in particular of foetuses and breast-fed neonates). This perchlorate equivalent background mostly consists of thiocyanate and nitrate in food and water.

Therefore, the true NOEL is the Greer apparent NOEL + the background perchlorate equivalent level (PEC) and is, at 157ug/kg-dayPEC, 22 times larger than the apparent Greer NOEL of 7 ug /kg-day. This leads to a PEC RfD of 15.7 ug/kg-day instead of the NAS RfD of 0.7 ug/kg-day.

This background level should be taken into account in evaluating whether regulation of perchlorate through the Safe Drinking Water Act would result in a meaningful opportunity for health risk reduction for persons served by public water systems, and in determining what constitutes a level of public health concern. For the reasons discussed below, regulation of perchlorate would not achieve either of these goals, because the effect on iodine uptake (the basis for the NOEL) resulting from perchlorate in public drinking water systems is inconsequential in comparison to the effect of other substances on iodine uptake. Due to the significant impact of these substances on iodine uptake,

even the elimination of perchlorate from the drinking water supply would result in (at best) only a negligible improvement in iodine uptake, and would have no effect on overall public health. If the purpose of the PHG is to be truly health protective, the perchlorate equivalent drinking-water PHG would need to be shared with those other goitrogens. For drinking-water, that would mean that the perchlorate PHG would need to be shared with the existing nitrate MCL.

Applying a default relative source contribution (RSC) of 20%, and assuming that the goal is to avoid the slightest iodine uptake inhibition caused by perchlorate and/or nitrate, we come to the conclusion that, even using the much higher NOEL level discussed above, to achieve the intended effect of the PHG, the MCL for nitrate would need to be drastically lowered (by more than 80 % if the perchlorate PHG were between 0 (zero) and 1 ppb and by more than 75% if the PHG were to be 15 ppb) and the vegetable and fruit intake of a large segment of the US population (all of the population with a balanced diet) would need to be limited to the daily consumption of fruit and vegetables equivalent to the nitrate content of 2.3 ounces of lettuce or equivalent to the thiocyanate + nitrate content of an even smaller amount of broccoli.

The logical conclusion of this analysis indicates that either the nitrate MCL is too high to avoid iodine uptake inhibition, or a NOEL based on iodine uptake inhibition is not an appropriate effect on which to base a PHG for perchlorate. Because foods containing nitrate and thiocyanate are an integral part of a healthy diet, and the effects on iodine uptake can be countered by adequate levels of iodine in the diet, logic dictates the latter conclusion.

This logical conclusion is further supported (if support would still be needed) by the fact that, as mentioned before; i) for women with insufficient iodine (<100 ug UI) the total goitrogen load and perchlorate background are about half, see study addendum 1; ii) according to the same NHANES database, urinary iodine is strongly and positively associated with urinary perchlorate which means that the more there is perchlorate background exposure the more there is background iodine exposure (see study addendum 2).

Response: See response to comment IDs 28529, 28551, and 20523 under comment code 2500 EPA cannot evaluate calculations that have not been peer reviewed. EPA believes the nitrate NPDWR appropriately derived.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0227
EPA Comment ID: 28821
EPA Comment Code: 2600

Comment: 1.2. Determination of the background adjustment factor, BAF

1.2.1. Epidemiological studies: Quantitative Observational Study versus Experimental Study

In order to arrive at an RfD, an effect level is normally determined. The effect level is determined by means of epidemiological studies. By far the most common type of human epidemiological study is the quantitative observational study, which is one of the two that leads to dose-response information [FN3: R.L. Calderon ,The Epidemiology of Chemical Contaminants of drinking Water , US EPA, Food and Chemical Toxicology, 38, 2000.] (and which cannot be controlled for substances that have

not been measured). The other type is the controlled experimental study and is typically used to evaluate drugs or vaccines, but is seldom used to evaluate environmental contaminants.[FN3: R.L. Calderon ,The Epidemiology of Chemical Contaminants of drinking Water , US EPA, Food and Chemical Toxicology, 38, 2000.]

The quantitative observational study is in fact a dose-response study of the background level of the contaminant (which in the case of perchlorate is assumed to be food and drinking water). This is not the case of an experimental study, where the dose-response of the administered dose is studied and not that of the background level. This type of study instead presumes that the background level of the substance is zero, and that the only cause of the effect of the substance in the bodies of the subjects is the administered dose of the substance.

Therefore, in an experimental study such as the Greer study, the effect level that would be found through such longitudinal experiment would not be the true effect level. Instead, the true effect level would be the sum of the administered dose and the background effect level. The Greer 2002 study from which the RfD was derived was such an experimental study, and the background perchlorate exposure level may have been confused with the administered dose or may simply have been overlooked. Indeed, experimental clinical studies on humans are, for obvious reasons, seldom done in order to estimate the dose- response of environmental contaminants. The Greer 2002 trial, however, had as its endpoint a Non Observable Effect Level, which was considered a non adverse effect level. This trial was, therefore, an inappropriate method to effectively determine the NOEL.

1.2.2. NIS Iodine uptake inhibitors have a cumulative effect

Normally the (adverse) effect level of each contaminant is established independently from other contaminants, as most toxins have a specific effect, their effect is not cumulative at all levels, or their cumulative effect is simply not well known. However, this is not the case for the NIS competitive iodine uptake inhibitors, or goitrogens, whose mode of action is well known and is known to be cumulative. Particularly for the three major goitrogens-- nitrate, perchlorate and thiocyanate -- their simple cumulative effect and their relative potency are well known. Thus, in the case of the Greer study, the background level is the perchlorate background level, plus the level of other goitrogens with the same mode of action, i.e. the (competitive) inhibition of iodine uptake.

1.2.3. The Background Adjustment Factor BAF

Indeed, the Greer participants did have additional perchlorate doses through background food and drinking water perchlorate as well as background perchlorate equivalent caused by other goitrogens. This means that the NOEL from the Greer experimental study and which we call Greer_NOEL is lower than the real NOEL which we call PEC_NOEL (Perchlorate Equivalent Concentration NOEL) with PEC_NOEL = Greer_NOEL x BAF (Background Adjustment Factor) and with BAF>1.

1.2.3.1. The perchlorate background adjustment

The median perchlorate background exposure in the US adult population is 4.6ug/day,[FN4: Blount BC, Valentin-Blasini L, Osterloh JD, Mauldin JP, Pirkle JL, 2006a. Perchlorate Exposure of the U.S. Population, 2001-2002. Journal of Exposure Science and Environmental Epidemiology, 1-8.] which is 0.066 ug/kg-day representing only 0.9 % of Greer- NOEL. Thus the mean total perchlorate

exposure of the Greer cohort = 7 ug/kg-day + 0.066 ug/kg-day = 7.07 ug/kg-day which for all practical purposes we round off and keep at 7 ug/kg-day.

It is worth noting here that the cross-sectional Blount et al, 2006 background study [FN5: Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell L, 2006b. Urinary Perchlorate and Thyroid Hormone Levels in Adolescent and Adult Men and Women Living in the United States. Environmental Health Perspectives 114(12): 1865-1871.] showed a weak but statistically significant relationship of this very low background exposure with an effect, and even more surprisingly a downstream adverse effect only. This same significant adverse effect relationship, however, is also shown to exist with the background level of some organo halogens in the same NHANES database but which are known, contrary to perchlorate, to cause that kind of weak adverse effect at such low levels.

1.2.3.2. Other goitrogen background adjustment

In addition, the Greer trial participants were exposed to a perchlorate equivalent background in food and drinking-water from the goitrogens thiocyanate (SCN), nitrate (NO3-) and other goitrogens affecting iodine uptake into the NIS such as fluoride, chlorate and several others. For practical purposes we will only take nitrate and thiocyanate into account as those two are the most important and best documented goitrogens (Michael Zimmermann, European Thyroid Association (ETA) Symposium, Lisbon, September 9, 2009).

In the US adult population, serum background exposure to nitrate expressed in serum perchlorate equivalent concentration (SPEC) is estimated at 0.167umol/l and that of thiocyanate at 1.333umol/l for a total of 1.567umol/l compared to a serum Greer_NOEL for perchlorate estimated at 0.070umol/l.[FN6: See Office of Inspector General Scientific Analysis of Perchlorate ,Assignment No. 2008-0010, December 30, 2008, page 84 and 85 (goitrogen serum and urinary levels based on the NHANES 2001-2002 dataset).] Thus, perchlorate serum exposure of 0.070 umol/L at the Greer NOEL dose represents only 4.5 % of the total serum goitrogen load of 1.567umol/L or in other words the perchlorate equivalent concentration NOEL, PEC_NOEL, which is the real NOEL, is 22.4 times larger than the Greer_NOEL(which itself is more than 100 times larger than the perchlorate background). PEC_NOEL = Greer_NOEL x BAF= Gr_NOEL x 22.4 = 157 ug /kg-day where BAF is a perchlorate equivalent BAF.

The Greer NOEL of 7ug/kg-day is not a true NOEL but a NOEL on top of the much larger (i.e. 21 times larger) perchlorate equivalent background level. Therefore, the true NOEL is the Greer apparent NOEL, plus the background equivalent perchlorate level, and is more than 22 times larger than the apparent Greer NOEL of 7 ug /kg-day. The background exposure level of perchlorate itself, however, is negligible as it is more than 100 times smaller than the Greer NOEL or more than 2,200 times smaller than the true NOEL, taking into account only the most well-known goitrogens.

1.2.4. The true reference dose RfD

The true RfD is obtained by dividing the true NOEL by UF (uncertainty factor) which NAS set at 10. Thus the true RfD or PEC_RfD = PEC_NOEL/UF = 157ug/kg-day /10 = 15.7ug/kg-day, equivalent with the ingestion of 2 litres of 550 ppb perchlorate drinking-water if there were no other goitrogen exposure from drinking-water, food and any other source.

1.2.5. From the true RfD to Perchlorate Equivalent Concentration PHG

To derive a PHG (Public Health Goal) or MCL (Maximum allowed Contaminant Level) for drinking-water from an RfD, usually a RSC (Relative Source Contribution) is applied.

Assume that 80% of perchlorate + nitrate + thiocyanate background originate from food and 20% from drinking-water. A 20 % RSC is the lowest and most conservative RSC used in the derivation of a maximum contaminant level goal [FN7: Regulatory Determination Support Document for selected Contaminants from the second Drinking Water Contaminant Candidate List (CCL-2), US-EPA report 815-D-06-007, December 2006.]. It is the minimum default value.

If no other goitrogens were present in drinking-water, the PHG would then be: 15.7 ug/kg-day x 70kg/2Lx 0.20= 110 ppb or again 22 times the 5 ppb proposed by for example NJ Department of the Environment which used the same 20 %RSC [FN8: http://www.nj.gov/dep/watersupply/perchlorate_mcl_10_7_05.pdf].

1.2.6. The perchlorate-only PHG in relation to the total perchlorate-equivalent PHG

If other goitrogens are present, a PEC_PHG (i.e. the total perchlorate equivalent PHG) should be shared with those other goitrogens. This approach is the only sensible approach, as no distinction between the goitrogens can be made if the goal of the MCL is to be health protective.

For drinking water, nitrate would be the most significant other goitrogen. If the current nitrate MCL were taken into consideration, then PEC_PHG should be equal to PHG of perchlorate + MCL of nitrate expressed in PEC (Perchlorate Equivalent Concentration)[FN9: Nitrate PEC = [nitrate]/240 when expressed in molar weight and /150 when expressed in weight: De Groef B, Decallonne BR, Van der Geyten S, Darras VM, Bouillon R, 2006. Perchlorate Versus Other Environmental Sodium/iodide Symporter Inhibitors: Potential Thyroid-related Health Effects. Eur J Endocrinol 155(1):17-25.].

As mentioned, the combined perchlorate + equivalent nitrate maximum level should be< 110 ppb or ([Nitrate] PEC+ [perchlorate] should be <110 ppb. Since the nitrate MCL = 44 ppm nitrate or 44,000/150ppb=293 ppb PEC, PE_PHG should be equal to PHG perchlorate + 293ppb. Hence, PHG perchlorate should be equal to 110 ppb-293 ppb= negative 183 ppb, which is of course not possible.[FN10: Note: if an RSC =1, as was the case for the nitrate MCL, would have been applied on the background perchlorate equivalent level as well, PEC_PHG would have been = (15.4 ug/kg-day) x 70kg/2 l x 1= 539 ppb. Indeed in determining the drinking water nitrate MCL no RSC (i.e. RSC=1) taking into account food has been applied even though nitrate levels in food such as vegetables are very significant (and as much significant in terms of BBS as iodine uptake inhibition).If this would have been done, it would on itself already have lowered substantially the nitrate MCL. A 0.2 default value, as we apply here for PEC, would have lowered it already to 8.8 ppm. According to the WHO (see ref. 12) the contribution of drinking-water to nitrate intake is usually less than 14 so even lower than the conservative 20 % default value assumed here.]

Thus, we must conclude that either the nitrate MCL is too high to avoid iodine uptake inhibition, or a NOEL based on iodine uptake inhibition is not an appropriate effect on which to base a PHG for perchlorate -- or both. If, nevertheless, the iodine uptake inhibition NOEL is to be kept as the

relevant effect, the nitrate MCL should be lowered in the first instance from 44 to 14.2 ppm to allow a perchlorate PHG of for example 15 ppb, the one EPA currently proposes as an interim level.

There is an additional background adjustment, another RSC, to be made for nitrate. Contrary to perchlorate and thiocyanate for which the serum exposure is proportional to the oral exposure, there is, besides an oral exposure, also an endogenous exposure to nitrate estimated at 45% of total nitrate exposure.[FN11: Nitrate and Nitrite in Drinking Water, Subcommittee on Nitrate and Nitrite in Drinking Water, Commission on Life Sciences, NRC (National Research Council), page 38. Washington, DC, National Academy Press, (ISBN-10: 0-309-08370-2).] Therefore there is an estimated relative source contribution of exogenous (oral) nitrate of 55% only. Thus to allow a perchlorate PHG of 15 ppb the nitrate MCL should be further lowered to 14.2 x 0.55= 7.8 ppm nitrate (or 2.1 ppm N as nitrate instead of 10 ppm N as nitrate) or about 1/5 of the current MCL). (This cannot be significantly compensated for by further lowering the perchlorate PHG from 15 to 1ppb (a 93% decrease), since this would only allow an increase of the nitrate MCL from 7.8 ppm to a still very low 9.9 ppm(a 27% increase only), still ending up with less than 1/4 of the MCL).

So, even with a PEC of 110 ppb (based on a true RfD of 15.5ug/kg-day PEC and a RSC of 20%), it is obvious that either the nitrate MCL (=293 ppb PEC) is too high to avoid iodine uptake inhibition or a NOEL based on iodine uptake inhibition is not an effect on which to base a PHG for perchlorate, or both.

Further, since we used a 20% default RSC which resulted in a perchlorate + nitrate MCL of 110 ppb for drinking-water, this means that the perchlorate equivalent exposure through drinking-water would be 2 Lx 110 ug/lL = 220 ug per adult /day. This would also mean that the intake through food, which would represent 80%, would be 220x80/20= 880 ug per adult/day perchlorate equivalent. This seems high on first sight but in reality is not as it represents an ingestion of only 66 g (2.3 ounce) of lettuce containing an ordinary 2000 ppm nitrate [FN12: Nitrate and nitrite in Drinking-water, Background document for development of WHO Guidelines for Drinking- water Quality, Originally published in Guidelines for drinking-water quality, 2nd ed. Addendum to Vol. 2 Health criteria and other supporting information. Word Health Organization, Geneva, 1998.]; (Hydroponic lettuce can contain up to 6000 ppm (40,000 ppb PEC) nitrate) or an even lower amount of broccoli (broccoli contains a mean of 11,500 PEC nitrate and 2000 PEC thiocyanate).[FN13: Perchlorate, Thiocyanate, and Nitrate in Edible Cole Crops (Brassica sp.) Produced in the Lower Colorado River Region, C. A. Sanchez, B. C. Blount, L. Valentin-Blasini,R. I. Krieger, Published online: 26 October 2007, Springer Science + Business Media, LLC 2007.]

Further, this also means that if the [perchlorate + nitrate] MCL were only 110 ppb PEC, consuming 66 g /day of lettuce and 2 litres of 110 ppb PEC DW would already represent the maximum allowed daily dose though water and food and no other nitrate carriers such as spinach, melon, cured meats and thiocyanate carriers such as broccoli and cauliflower, (which in themselves cause an average 8 times higher exposure load than nitrate)[FN14: Office of Inspector General, Scientific Analysis of Perchlorate, Assignment No. 2008-0010, December 30, 2008.] could be consumed that day by a healthy adult. Besides that, the nitrate level of the water consumed the same day could not exceed 1/5 of the current MCL if a perchlorate PHG of only 15 ppb would be chosen and 1/4 if a perchlorate PHG of 1 ppb would be chosen, as shown above.

Since in the US about half of the groundwater exceeds 10 ppm perchlorate and 6 % of groundwater exceeds 20 ppm[FN15: See ref. 12.] and almost all DW exceeds 1/5 of the MCL, the conclusion

should be that if a 15ppb or lower MCL for perchlorate is determined, the US population should basically stop consuming drinking water derived from groundwater and vegetables and fruit containing thiocyanates and nitrates. Even bottled water would not help much as almost all contain more than 5 ppm nitrate (based on a quick supermarket inquiry by the author) or 33 ppb PEC. Even "pristine", expensive imported bottled water contains between 3 and 10 ppm nitrate or up to 66 ppb perchlorate equivalent.

Conclusion

The NAS RfD, derived from the Greer NOEL is not a true RfD, since the Greer NOEL does not include the perchlorate equivalent background. The true RfD, at 15.5ug/kg-day, is more than 22 times larger than the NAS RfD of 0.7ug/kg-day.

Even at this higher RfD, however, the impact of other goitrogens, such as nitrate, in drinking water and food and thiocyanate in food would make it impossible for any level of perchlorate regulation to have any meaningful impact on public health. One reason for this may be that the appropriate "effect" to be considered in the evaluation of a NOEL should not be the point of iodine uptake inhibition, since the contribution of nitrate and even more of other goitrogens such as thiocyanate already largely exceeds the level of iodine uptake inhibition in healthy diets. Based on the foregoing, EPA is unable to demonstrate two of the three criteria required to regulate perchlorate in drinking water - namely: (1) EPA cannot demonstrate that perchlorate will occur in public water systems at levels of public health concern, because it cannot accurately be determined what constitutes a level of public health concern based on the current studies, and (2) EPA is unable to demonstrate that regulation of perchlorate represents a meaningful opportunity for health risk reduction for persons served by the public water system, since even its elimination would not result in any meaningful improvement in public health.

Response: Please see the response to comment ID 28819 under comment code 2600.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0227
EPA Comment ID: 28823
EPA Comment Code: 2600

Comment: ADDENDUM 1

By: Herwig Opdebeeck, SM, Opdebeeck Consulting

The unexpectedly weak goitrogen load of the iodine-deficient female US population

The U.S. iodine insufficient female population, besides an inadequate iodine containing diet, seems to have a generally unbalanced diet characterised by a low consumption of vegetables.

We refer again to the NHANES 2001-2002 data on urinary perchlorate (CLO4), nitrate (NO3), thiocyanate (SCN) and iodine where we show the relationship between iodine and total goitrogen load (TGL).

Table 1, 2, 3: NHANES 2001-2002: Relationship between iodine and total goitrogen load (TGL) (sorted for T4) [see PDF docket ID EPA-HQ-OW-2009-0297-0227]

The first table is for women with <100 ug/l urinary iodine (women<100), n=384), the second for women with >100 ug/l urinary iodine (women>100, n= 725), the third for the total population (n=2080) (Individuals with >2000 ug/l urinary iodine have been removed).

From these tables the following observations can be made:

Preliminary note: The serum goitrogen load is a measure for the effective thyroid goitrogen load. Here we refer to the urinary (U) load which does not accurately reflect the effective serum load. For example the residence time of thiocyanate is much longer than the one of nitrate or perchlorate. However this does not matter here since the purpose is only to compare the urinary loads between the different population groups i.e. the relative loads and because we can assume that urinary loads are proportional to serum loads (for example a double urinary load also means a double serum load).

-Women with iodine levels < 100 have a total goitrogen load(TGL) expressed in PEC that is about 50% lower than women > 100 and than the overall population (columns 9).

-Split into the constituents, their perchlorate, nitrate and thiocyanate levels, over the entire T4 spectrum (Col. 2), are about 50%, 50% and 35% lower respectively (columns 8, 5 and 7).

- This means that women with insufficient iodine levels happen to be those that are least susceptible to iodine uptake inhibition, if they would have been iodine sufficient.

-Urinary(U) perchlorate for all population groups represents less than 1% of the total urinary goitrogen load expressed in PEC (columns 10) and, as shown in section 1 above, also of the total serum(S) load.

Conclusion

Women with insufficient iodine levels happen to be those that are least susceptible to iodine uptake inhibition, if they would have been iodine sufficient. Improving their diet and iodine uptake would be the remedy.

Lowering instead the perchlorate intake by any rate (1, 10 or 100%) would not diminish NIS iodine uptake inhibition, also not for iodine-insufficient (<100) women since the NIS iodine uptake inhibition potential caused by TGL which is more than 100 times larger, is already 50 % lower than for iodine sufficient women (>100). So besides the fact that eliminating all perchlorate even the background level would still leave 99% of TGL untouched, this remaining 99% is only half that of iodine sufficient women.

ADDENDUM 2

By: Herwig Opdebeeck, SM, Opdebeeck Consulting

The strong relationship of low levels of U-perchlorate with U-iodine levels

In continuation of Addendum 1 : Nevertheless women with urinary iodine < 100 ug/l have a ratio of iodine to total goitrogen load (TGL) equal to about 0.2/1 for every T4 octille (1/8) while women > 100 ug/l have about a ratio equal to 0.8/1 also for every T4 octille (columns 13 of above 2 first tables of addendum 1) which means that, even though the goitrogen load for iodine-insufficient women is only about half that for iodine sufficient women, their iodine inhibition potential is 4 times higher so it is obvious that if iodine uptake inhibition in this subpopulation would occur it would be due to lack of iodine and not due to goitrogen load.

For perchlorate this is even more explicit since perchlorate, at low levels, is strongly related to iodine: see next figure[FN16: 1. Charnley G, Perchlorate: Overview of Risks and Regulation. Food and Chemical Toxicology, 2008. 2. Soldin OP, Tractenberg RE, Pezzullo JC. Do thyroxine and thyroid-stimulating hormone levels reflect urinary iodine concentrations? Therapeutic Drug Monitoring. 2005, 27: 178-185.] (fig.2) which is derived from the same NHANES 2001-2002 survey.

Fig 2 Relationship between urinary iodine and urinary perchlorate for the general population controlled for gender, T4 and TSH, p<0.0001 (ug/l, log scale) [see PDF docket ID EPA-HQ-OW-2009-0297-0227]

This relationship also suggests that low levels of perchlorate are naturally linked to iodine (both are formed in the atmosphere and both are found in naturally nitrate -rich soils in the US S-W deserts and arid regions).

So women with low natural background levels of perchlorate have low natural background levels of iodine. For higher background levels of perchlorate the link with iodine ceases to exist or not enough data points exist for those higher levels.

Thus it seems that women with higher levels of iodine not only tend to have higher levels of natural perchlorate but additionally some from other contaminated (point) sources.

For the other 2 goitrogens this suggests that those iodine-insufficient women also consume significantly less vegetables than the iodine-sufficient population. This could then also explain the higher non-natural levels of perchlorate from vegetables irrigated with synthetic perchlorate containing water such as the Colorado River (or, as mentioned before, this non- relationship can be due to a lack of data points at those higher levels). Nevertheless those synthetic perchlorate levels are themselves still insignificant compared to the total goitrogen load.

All this strengthens once more the argument that in the US population the potential iodine uptake inhibition does not lay with goitrogens and even less with perchlorate but clearly with a lack of iodine.

Conclusion - Even though the goitrogen load of iodine insufficient women is only about half that of goitrogen sufficient women, their ratio iodine to goitrogen load is much lower which suggests once again that the remedy is iodine. - For low background levels of perchlorate there seems to exist a remarkable relationship with iodine which suggest that those lower levels are natural levels since synthetic perchlorate such as rocket fuel does not contain iodine. - It is once again suggested here that Iodine insufficient women seem to have also a diet low in vegetables besides a diet low in iodine containing food such as fish.

Response: EPA cannot evaluate calculations that have not been peer reviewed.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28878
EPA Comment Code: 2600

Comment: Fifth, the level of IUI that would be associated with exposure to perchlorate at the RfD is minimal compared to the IUI associated with other environmental goitrogens naturally present in many foods. Nitrate and thiocyanate are less potent (Tonacchera et al., 2004) but more plentiful inhibitors of NIS activity than perchlorate (Belzer et al., 2004). The potency of nitrate and thiocyanate relative to perchlorate has been demonstrated in vivo (Wyngaarden et al., 1952, 1953; Greer et al., 1966; Belzer et al., 2004) and in vitro (Tonacchera et al., 2004). When based on perchlorate equivalence, the effects of perchlorate are much smaller than the effects of either nitrate or thiocyanate (Belzer et al., 2004; U.S. EPA, 2008b). The potential for perchlorate to inhibit iodide uptake cannot be distinguished from the effects of other NIS inhibitors (De Groef et al., 2006). Because exposure to nitrate and thiocyanate would continue, the premise underlying EPA's attempt to isolate the effect of perchlorate is limited in its ability to provide an actual public health benefit.

Response: See response to comment IDs 28529 and 28551 under comment code 2500.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28889
EPA Comment Code: 2600

Comment: One major scientific issue is that the effects of agents that affect IUI in the same way as perchlorate were not considered by the Notice.

Because perchlorate, nitrate, and thiocyanate compete with iodine for uptake by the NIS, the combination of these chemicals in food or water will affect iodine uptake to the thyroid as well as absorption into the body from the gut. The NIS is located in the small intestine and uptake of iodine can be reduced by sufficient doses of perchlorate (Brown-Grant, 1961). In defining a HRL, it is assumed that 100% of an ingested dose is able to reach the thyroid. Of the four chemicals (perchlorate, nitrate, thiocyanate, iodine), perchlorate has the highest affinity for the NIS, however, the other three are more abundant in the diet. In the FDA Total Diet Study, the dose range of perchlorate was 2.4 to 9.1 ug/person-d and the dose range of iodine was 144 to 353 ug/person-d (Murray et al., 2008). Similar to biomonitoring studies (Blount et al., 2006) and dose models (Belzer et al., 2004), the OIG Draft Report (U.S. EPA, 2008b the results for exposures to nitrate, thiocyanate, and perchlorate found that perchlorate accounted for less than 1% of the predicted IUI in the total goitrogen load. Based on NHANES 2001-2002, the average urinary concentration of perchlorate was 4.8 ug/L, which was much lower than the urinary concentrations of nitrate, thiocyanate, and iodine at 55,017 ug/L, 2,042 ug/L, and 200 ug/L, respectively. Figure 2 demonstrates the relative contribution of perchlorate to total goitrogen load using another set of data, the NHANES 2001-2002 database.

Figure 2. Total goitrogen load in perchlorate equivalence* based on urinary measurements from women ages 12 and older from NHANES 2001-2002.** [see PDF docket ID EPA-HQ-OW-2009-0297-0662]

One characteristic of this relationship is that as perchlorate dose increases in food, so does intake of nitrate, thiocyanate, and iodine. Figure 2 presents the cumulative intake of the four agents based on NHANES data using perchlorate equivalence of the urinary concentration of nitrate and thiocyanate. Two things become clear. First, as iodine level increases, so does total cumulative dose. Second, perchlorate contributes, by far, the smallest amount to total cumulative dose. The chart shows that as the goitrogen load increases, people tend to have increased intake of iodine, probably due to greater ingestion of total food.

Response: See response to comment ID 28529 under comment code 2500.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group (EWG)
EPA Document ID: EPA-HQ-OW-2009-0297-0499
EPA Comment ID: 28928
EPA Comment Code: 2600

Comment: Background: Perchlorate is unique among chemical contaminants for its ubiquity- it has been found as a contaminant in drinking water in at least 26 states, in 74% of nearly 300 types of commonly consumed foods and beverages tested by the Food and Drug Administration (FDA), and in the urine of 100% of Americans tested by the Centers for Disease Control and Prevention (CDC) (GAO 2005, Blount et al 2006a, Murray et al 2008). Its primary clinical effects are on the thyroid gland, where it can disrupt the production of thyroid hormones that are critical for normal brain development and growth in the fetus, infants, and children. Perchlorate inhibits thyroid hormone synthesis by preventing iodine, the building block for thyroid hormones, from being taken up into the thyroid gland from the circulation. Iodine status is especially important in determining vulnerability to perchlorate, as confirmed by a recent large-scale epidemiological study from the CDC that found that women with lower iodine levels had more significant changes in thyroid hormone levels associated with environmental perchlorate exposure when compared with women with higher iodine levels (Blount et al 2006a).

Response: EPA agrees that individuals with inadequate iodide nutritional status are more likely to be adversely impacted by perchlorate.

EPA Comment Code: 3000 Perchlorate Occurrence in Drinking Water

Individual Comments
Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0469
EPA Comment ID: 19899
EPA Comment Code: 3000

Comment: Does the EPA's decision not to regulate perchlorate in drinking water mean that it accepts an exposure of 420 ppb in Utuado, Puerto Rico, or has that town's water supply been thoroughly inspected and all water sources with more than 15 ppb have been shut down?

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Diane VanDe Hei
Commenter Organization: AMWA
EPA Document ID: EPA-HQ-OW-2008-0692-1525
EPA Comment ID: 20446
EPA Comment Code: 3000

Comment: Other Considerations

AMWA believes that factors other than those discussed in the notice need to be considered. The contamination of water supplies by perchlorate is on-going and spreading unlike many other CCL contaminants where a determination not to regulate has been made, such as in the case of pesticides that are no longer used and have low and decreasing occurrence levels. Perchlorate, on the other hand, is expected to have increasing occurrence levels and impact increasing numbers of water systems - clearly a call for at least the actions outlined herein.

AMWA appreciates the opportunity to comment on EPA's preliminary regulatory determination. If EPA has any question about our comments please do not hesitate to contact me or Erica Brown, Director of Regulatory Affairs, at 202-331-2820.

Sincerely,

Diane VanDe Hei Executive Director Cc: Cynthia Dougherty, OGWDW Eric Burneson, OGWDW

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120. Regarding perchlorate contamination of water supplies, EPA acknowledges that some systems may have had an increase in perchlorate occurrence. The Agency analyzed the additional information and decided that regulation of perchlorate due to occurrence and health implications was warranted.

Commenter Name: Mark S. Mayer

Commenter Organization: South Dakota Department of Environment & Natural Resources (DENR)
EPA Document ID: EPA-HQ-OW-2009-0297-0467
EPA Comment ID: 28483
EPA Comment Code: 3000

Comment: - Comments on interpreting occurrence data - Because South Dakota does not have any occurrence data, a new rule for Perchlorate would be another regulatory burden for our drinking water systems, but it would result in no positive health benefits for their customers.

Response: Using the criteria mandated by the 1996 SDWA Amendments EPA has determined that regulation of perchlorate in drinking water systems presents a meaningful opportunity to reduce health risk for persons served by public water systems. See response to comment code 6120.

Commenter Name: Andria Ventura
Commenter Organization: Clean Water Action et al.
EPA Document ID: EPA-HQ-OW-2009-0297-0528
EPA Comment ID: 28512
EPA Comment Code: 3000

Comment: Perchlorate has been found in over 400 drinking water sources in 26 states, potentially affecting tens of millions of people. EPA's own data say that nearly 17 million people receive their water from public water systems where perchlorate has been found at levels exceeding 4 ppb. Were sampling routinely conducted with a detection limit of 1 ppb, that number would be much higher- particularly considering the estimated 20 million people in the Southwest who receive drinking water from the Colorado River.

Response: EPA estimates that at least 5.1 to 16.6 million people are served by PWSs, for which we have data, that have perchlorate contamination. EPA has determined that a NPDWR for perchlorate could reduce perchlorate exposures for these populations to levels below the potential alternative HRLs that EPA has identified as levels of public health concerns for purposes of this determination, and that such exposure reductions present a meaningful opportunity for the reduction of health risks for persons served by PWSs.

Commenter Name: Kathy Curtis
Commenter Organization: Alliance of Nurses for Healthy Environments (ANHE)
EPA Document ID: EPA-HQ-OW-2009-0297-0651
EPA Comment ID: 28543
EPA Comment Code: 3000

Comment: Perchlorate has been found in more than 400 drinking water sources in 26 states, potentially affecting tens of millions of people. EPA's own data say that nearly 17 million people receive their water from public water systems where perchlorate has been found at levels exceeding 4 ppb.

Response: See response to comment ID 28512 under comment code 3000.

Commenter Name: Tom Porta

Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 28747
EPA Comment Code: 3000

Comment: 4. The collection of new data for perchlorate in public water systems would provide reliable occurrence data to inform the establishment of a national primary drinking water standard. The need for new occurrence data is underscored by the significant improvements in water quality (considerably lower perchlorate concentrations) within the Lower Colorado River System since the UCMR 1 data were collected between 2001 and 2005. Additionally, newer and more sensitive analytical methods are now available that would permit perchlorate analysis with reporting limits (detection limits) at or below 1 ug/L. Consequently, the new occurrence data would represent a more robust data set that would permit statistical analysis without the inherent limitations present in the current Bayesian modeling of the existing, outdated occurrence data.

Response: EPA acknowledges that there are newer and more sensitive analytical methods that are now available that would permit perchlorate analysis with reporting limits at or below 1 ug/L. The Agency does not believe that additional monitoring data is needed to determine that perchlorate meets SDWA's criteria for regulating a contaminant. EPA's UCMR data is nationally representative and sufficient for estimating the frequency and level of perchlorate contamination. In addition, the Agency plans to further evaluate perchlorate occurrence as part of the proposed national primary drinking water regulation.

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 28754
EPA Comment Code: 3000

Comment: Comment C.4.a.2: The NDEP recommends EPA require collection of new occurrence data to support the latter two of the three criteria that EPA most demonstrate in order to regulate this contaminant in drinking water; namely: (1) the contaminant is known to occur (or there is a substantial likelihood that the contaminant will occur) in public water systems, with a frequency and at levels of public health concern; and (2) regulation of such a contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems. The existing occurrence data are both outdated and nonrepresentative of current conditions.

The Unregulated Contaminant Monitoring Program is designed to collect such data for use in evaluating and prioritizing contaminants on the Drinking Water Contaminant Candidate List. It is an established program to "help ensure that future decisions on drinking water standards are based on sound science" (www.epa.gov/safewater/ucmr/ucmr1/factsheet.html#list). Perchlorate was on the analysis list published for the first Unregulated Contaminant Monitoring Rule (UCMR 1) in 1999 to collect data from 2,800 large public water systems and 800 small public water systems throughout the United States, but as further discussed elsewhere herein, the data is now largely obsolete due to analytical method changes and perchlorate remediation work in the Southwest. The NDEP recommends that EPA consider use of the established and successful UCMR process to collect updated national public water system occurrence data.

The NDEP believes use of outdated (historical) occurrence data collected from 2001 through 2005 would be inappropriate because the quality of source water from the Lower Colorado River System has improved as a result of several successful remediation projects in the Las Vegas Valley. This source water provides the water supply for a large portion of the US population (approximately 26 million US residents) and for a large amount of irrigated vegetable crops. The current perchlorate concentrations in the Lower Colorado River System are significantly lower than the concentrations present when the occurrence data were collected (2001 - 2005). The NDEP believes that collection of new occurrence data would permit a more accurate assessment of the exposure scenario and lead to a conclusion that regulation of perchlorate under the Safe Drinking Water Act (SDWA) does not present a meaningful opportunity for health risk reduction for persons served by public water systems or through ingestion of the referenced irrigated crops. The following summary of perchlorate remediation efforts within the Las Vegas Valley and corresponding water quality improvements within the Lower Colorado River system are provided to support this comment.

Response: EPA disagrees with the statement that UCMR 1 data is obsolete. The UCMR 1 includes sample results reported by 3,865 public water systems between 2001 and 2005. This is the best available data collected in accordance with accepted methods on perchlorate. EPA recognizes that changes in perchlorate levels may have occurred in water systems since the UCMR samples were collected. However, EPA does not believe that the regulatory determination should be further delayed when we have a robust data set that can be used to evaluate occurrence. EPA plans to further analyze available perchlorate data in developing a proposed drinking water regulation.

EPA Comment Code: 3100 UCMR 1 occurrence analysis

Individual Comments
Commenter Name: Ed Thomas
Commenter Organization: National Rural Water Association (NRWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0163
EPA Comment ID: 20271
EPA Comment Code: 3100

Comment: First, Phillips and Chambless,(see reference 1 electronic attachment - "Phillips compliance data variability.pdf") [see PDF of docket ID EPA-HQ- OW-2007-0068-0163] evaluated compliance data for several contaminants obtained from a cross section of state regulatory agencies and found consistently large variability in the means of quarterly samples taken for compliance purposes. This variability, expressed as the standard error of the mean divided by the mean, is significant enough (100% or more in many cases) to call into question the validity of decisions made based on these data. There is no reason to assume that the quality of the occurrence data from the UCMR effort would be any better than the quality of these compliance data, and NRWA strongly recommends that EPA resolve this quality issue before trying to make CCL2 regulatory decisions that are based on rather precise calculations of occurrence levels times the number of persons exposed.

Response: EPA respectfully disagrees with NRWA on the assertion that the validity of occurrence data from UCMR be compromised based upon an analysis of variability in compliance monitoring data collected by public water systems. UCMR has gone under rigorous QA/QC measures to ensure that data variability is at a minimum. A detailed description of UCMR monitoring can be found in the Federal Register under docket number EPA–HQ–OW–2007–0068. The title of the reference that describes UCMR is "The Analysis Of Occurrence Data From The First Unregulated Contaminant Monitoring Regulation (UCMR 1) In Support Of Regulatory Determinations For The Second Drinking Water Contaminant Candidate List".

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1748
EPA Comment ID: 20656
EPA Comment Code: 3100

Comment: Fifth, EPA has extensive monitoring data from public water systems on perchlorate occurrence in drinking water. While your November 5th letter [See PDF Docket ID EPA-HQ-OW-2008-0692-1749] states perchlorate has "wide occurrence," EPA's UCMR 1 data suggests that drinking water perchlorate occurrence is much less frequent that other compounds (sodium, manganese, sulfate, and boron) for which EPA has determined Federal drinking water standards are not necessary. The monitoring data also show that, for an overwhelming majority of the US population served by public water systems, exposure to perchlorate in drinking water is at a concentration much less than EPA's calculated HRL of 15 ppb. In fact, based on UCMR1, only 1.8% of public water systems had levels of perchlorate that were above the minimum reporting limit of 4 ppb.[FN8: US EPA, Unregulated Contaminant Monitoring Regulation 1 List 1 Assessment

Monitoring, 1999.] Although unpublished, the EPA's merger of the NHANES-UCMR1 datasets study has been peer-reviewed.

Response: Administrator Stephen Johnson replied to the SAB on January 9, 2009. The letter is available in EPA's docket ID No. EPA-HQ-OW-2009-0297 for this notice. EPA disagrees that only 1.8% of public water systems had levels of perchlorate that were above the minimum reporting limit. In the October 2008 FR notice, EPA presented information on the drinking water occurrence of perchlorate. The data source was EPA's UCMR 1 and the samples were collected between 2001 and 2005. A total of 34,331 samples were collected from 3,865 public water systems. EPA found that 4.1% of the systems (160 out of 3,865 systems) reported perchlorate at, or above, the MRL of 4ug/L.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-2082
EPA Comment ID: 21027
EPA Comment Code: 3100

Comment: 10. Also regarding UCMR sampling, your letter questions the UCMR sampling because it focused only on large PWSs and does not account for exposure from "local hot spots" due to blasting, fireworks, and industrial and military releases.

The UCMR is the most complete source of information on contaminant occurrence in the nation's drinking water sources. The process for collecting data on unregulated contaminants in large as well as small water systems has been well established and relied upon by EPA for regulatory determinations from both the Contaminant Candidate List (CCL) 1 (issued July 2003) and CCL 2 (issued July 2008). Additionally the National Rural Water Association, a non-profit federation of state rural water associations (and has the largest utility membership) expressed support for EPA's preliminary determination, stating "the Agency has relied on sound science" in making its decision."[FN9: National Rural Water Association, Drinking Water Preliminary Regulatory Determination on Perchlorate (Docket Number: EPA-HQ-OW-2008-0692), Nov. 10, 2008.]

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Ellen Blaschinski, M.B.A., R.S.
Commenter Organization: Regulatory Services Branch, Connecticut Department of Public Health
EPA Document ID: EPA-HQ-OW-2008-0692-2091
EPA Comment ID: 21116
EPA Comment Code: 3100

Comment: Public supplies in Connecticut were tested for perchlorate as part of the 2001 Unregulated Contaminant Monitoring Rule (UCMR) round of testing. There were no detections in those systems at that time. However, that is a snapshot and not nearly the complete and ongoing surveillance that a federal MCL would provide. We note that the parallel UCMR testing in Massachusetts found very few detections of perchlorate and yet additional testing by the State of Massachusetts found substantial public water contamination on a site-related basis. Additional testing in Connecticut is warranted given the changing use pattern of perchlorate in blasting materials, fireworks and other applications.

Response: See response to comment ID 29097 under comment code 3100 and response to comment code 6120.

Commenter Name: Kay Brothers
Commenter Organization: Southern Nevada Water Authority
EPA Document ID: EPA-HQ-OW-2009-0297-0667
EPA Comment ID: 28700
EPA Comment Code: 3100

Comment: It is important for EPA to properly characterize its estimates of the potential population exposed to perchlorate. Perchlorate cleanup along the Colorado River has been very successful in recent years, and this represents the water supply for 26 million people in the Southwest. Perchlorate was detected in the Las Vegas Wash in 1997. The contamination was due to past disposal practices at the perchlorate manufacturing sites in the Las Vegas valley. Due to efforts of the manufacturers, Tronox LLC (Kerr-McGee Chemical LLC) and American Pacific Corporation, working with the Nevada Division of Environmental Protection, perchlorate concentrations entering Lake Mead and the lower Colorado River System have decreased dramatically. The perchlorate load entering Lake Mead in 1998 was 1013 lbs/day; it has been currently reduced to 61 lbs/day.

Perchlorate concentrations have also decreased dramatically in the drinking water since 1998 throughout the lower Colorado River system. The average perchlorate concentration reported by the Authority and the City of Henderson for the Unregulated Contaminate Monitoring Rule (UCMR) averaged 9.6ug/L and 2.9 ug/L, respectively. Currently, the perchlorate concentration in the Authority and the City of Henderson's drinking water is an average of 2.1ug/L. Drinking water providers along the lower Colorado River have reported similar decreases in perchlorate concentrations. The data collected for the UCMR may not reflect current perchlorate exposure for the Southwest. The average perchlorate concentration at Whitsett Reservoir for the last two years is 1.6 ug/L. This is the Colorado River source water for the Metropolitan Water District of Southern California and the Central Arizona Project. California and Arizona blend with instate waters which result in a lower concentration. Three states have adopted perchlorate standards of 6 ug/L or less, which requires the water wells to be shut down if above the state limit. The exposure to perchlorate has been reduced significantly in the Southwest.

If you have any questions about these comments, please do not hesitate to contact me at 702-862-3708 or Shane Snyder at 702-856-3668.

Sincerely, Kay Brothers Deputy General Manager Engineering and Operations

KB/df Enclosure

Reference:

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Response: EPA is aware of perchlorate cleanup along the Colorado River and believes that it has properly characterized the estimate of population exposed to perchlorate in drinking water. See response to comment ID 28856 under comment code 3100.

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 28756
EPA Comment Code: 3100

Comment: Consequently, the NDEP believes use of outdated (historical) occurrence data collected from 2001 through 2005 would be inappropriate because the source water (Lower Colorado River System) for a large portion of the US population and for a large amount of irrigated vegetable crops has substantially improved as a result of several successful remediation projects in the Las Vegas Valley. The current perchlorate concentrations are significantly lower than the historical concentrations when the occurrence data were collected (2001 - 2005). Moreover, current concentrations of perchlorate in the Lower Colorado River System are less than health-protective levels for the approximately 26 million US residents who use this water for drinking water and numerous agricultural operations for irrigating crops. The NDEP believes that collection of new occurrence data would provide for a more accurate assessment of the exposure scenario applicable to this large segment of the US population, and lead to a conclusion that regulation of perchlorate under the SDWA does not present a meaningful opportunity for health risk reduction for persons served by public water systems or consuming the above-referenced irrigated crops.

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Response: See response to comment ID 28856 under comment code 3100 and ID 28754 under comment code 3000.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28839
EPA Comment Code: 3100

Comment: With respect to using UCMR data to estimate concentrations above 4 ug/L, again AMWA urges EPA to recognize that occurrence in finished water at many water systems has decreased.

Response: See response to comment ID 28856 under comment code 3100.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0415
EPA Comment ID: 28856
EPA Comment Code: 3100

Comment: Current National Exposure to Drinking Water Perchlorate

AWWA believes that the population exposed to perchlorate that was indicated by EPA's UCMR1 data is no longer valid. In an informal survey conducted by AWWA, we found that many sources that had detected perchlorate from UCMR1 monitoring are either no longer being used or are being treated per the requirements of maximum contaminant levels (MCL's) established in California and Massachusetts. Additionally, successful treatment of the perchlorate source to Colorado River contamination has lowered concentrations to below 4 ug/L. AWWA believes that EPA would be well served to work with state primacy agencies to evaluate the 160 water systems with perchlorate

detections from UCMR1 to determine the actual national population currently exposed to perchlorate above 4 ug/L. AWWA believes this information will further help inform EPA as to whether there is a meaningful opportunity for health risk reduction by regulating perchlorate.

Response: EPA acknowledges that there may be changes (increasing or decreasing) in the levels of perchlorate in public water systems since the UCMR data were collected from 2001 to 2005. EPA believes the UCMR data are best available data collected in accordance with accepted methods on the frequency and level of occurrence in drinking water. Therefore EPA is basing its occurrence evaluation on these collected data for the regulatory determination and will further evaluate perchlorate occurrence as part of the proposed rulemaking.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28870
EPA Comment Code: 3100

Comment: 3. Use of data on perchlorate occurrence in drinking water: The occurrence analysis presented in the Notice relies on data that are nearly a decade old and it assumes exposure to maximum concentrations detected anywhere within a public water system (PWS), even in untreated source water. Therefore, the analysis most likely overestimates concentrations of perchlorate in drinking water. Additionally, the Notice's estimates of populations exposed to perchlorate are overstated because it assumes the entire population served by a PWS is exposed to the maximum concentration, even if the detection was in untreated source water, and it overlooks the steps that have been taken- particularly in California, Massachusetts and New Jersey-that substantially reduce the national population that may be exposed to environmental levels of perchlorate. The process the Notice followed to develop the estimated populations is not transparent, and as a result, it is not possible to independently calculate the estimated values in the Notice based on the information given. Independent calculations resulted in estimated population sizes that are about half of the Notice's estimates, even when conservative assumptions were used. EPA should use more current data to estimate occurrence as levels in drinking water have decreased since UCMR1 monitoring.

Response: See response to comment ID 28856 under comment code 3100 in regards to changes in the levels of perchlorate occurrence. With respect to EPA's evaluation of populations exposed to perchlorate, the Agency has presented analyses as part of its October 2008 Federal Register Notice, August 2009 Federal Register Notice, and the Final Federal Register Notice that explains EPA's estimation of populations potentially exposed to perchlorate. Using the UCMR 1 data, EPA took into account the potential for overestimating populations exposed to perchlorate using UCMR 1 monitoring data in which one can assume that the entire population served by a PWS is exposed to the maximum concentration from a single detection. Therefore, to respond to this concern, EPA also developed a central value estimate by assuming the population was equally distributed among all entry points and added only the proportion of the total population served by those entry points in a PWS that had at least one sample with perchlorate concentrations greater than the HRL being evaluated.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662

EPA Comment ID: 28890
EPA Comment Code: 3100

Comment: C. Use of Data on Perchlorate Occurrence in Drinking Water

To estimate how many people potentially could be exposed to perchlorate in drinking water, EPA used data from its first cycle of the UCMR1 (http://www.epa.gov/safewater/ucmr/ucmr1/index.html). The Notice presents the resulting population estimates in Table 3. The Agency estimated the size of the population exposed to perchlorate at different threshold levels (4 ug/L or higher, 5 ug/L or higher, etc.) by assuming that the entire population served by a public water system (PWS) is exposed to perchlorate at concentrations above a threshold level if at least one sample collected in the PWS contained perchlorate at or above the threshold level (even if all other samples are lower, or nondetect). Based on this assumption, the Notice reports an estimate of 16.6 million (M) people exposed to perchlorate at concentrations above the method reporting limit (MRL) of 4 ug/L. In addition, the Agency developed an alternative assessment by assuming that populations served by PWSs are equally distributed among entry points to the PWS and that only those portions of the population served by entry points with reported concentrations above the threshold are exposed. Based on this assumption, the Notice reports an estimate of 5.1M people exposed to perchlorate at concentrations above the MRL of 4 ug/L.

The Notice asks for comment on three general questions regarding the use of occurrence data to estimate exposure to perchlorate. Responses to these questions, based on the best available scientific information, follow.

Response: No response necessary to this summary of EPA information.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28892
EPA Comment Code: 3100

Comment: Scientific and statistical concerns with the Notice's use of the UCMR1 data set include the following:

* UCMR1 covers the years 2001 to 2005; some of these data are nearly a decade old. Data collected during this time overestimate current concentrations of perchlorate in drinking water. Guidelines EPA has established since 1992, including interim guidance for remediation and water exposure levels, and remediation of contaminated sites by responsible parties, have resulted in reductions in perchlorate levels in ground and surface water. For example, public information shows that annual average concentrations of perchlorate at the Las Vegas drinking water intake in Lake Mead declined almost 60% between 2000 and 2004 (from 13.1 ppb to 5.6 ppb), and the annual average concentrations in the Metropolitan Water District Colorado River Aqueduct intake at Lake Havasu on the Lower Colorado River declined about 50% between 2000 and 2004 (from 6.4 ppb to less than 4 ppb), and in 2004 nine of the twelve monthly samples were at levels too low to detect (i.e., below 4 ppb) (http://www.epa.gov/region/toxic/perchlorate/per_nv.html). The Colorado River

supplies water for agriculture in Arizona and California as well as drinking water for Southern California.

* Environmental exposure levels of perchlorate are declining. Although not an occurrence study, a recent study reports that urinary concentration of perchlorate is lower in NHANES 2003-2004 participants compared to NHANES 2001-2002[FN15: NHANES 2001-2002 is the basis for the study by Blount et al. (2006). See following section for the full discussion on Blount et al. (2006).] suggesting population exposure was lower during 2003-2004 (Mendez et al., 2009).

* Examination of the UCMR1 data set demonstrates that several major U.S. cities did not detect perchlorate in their drinking water. These cities are large metropolitan areas with corresponding large populations and include Washington DC, New York City, Newark, Baltimore, Philadelphia, Pittsburgh, Minneapolis/ St. Paul, Chicago, Milwaukee, Detroit, Cleveland, Indianapolis, Memphis, Nashville, Atlanta, St. Louis, San Francisco, Seattle, and Portland. Perchlorate is not ubiquitous in drinking water, but areas of detection appear to be regionalized. This does not diminish the importance of perchlorate where it has been detected at levels above the MRL (4 ug/L). States where significant perchlorate is present, e.g., California, have either promulgated drinking water standards or adopted EPA interim guidance. As a result, the trend of occurrence is toward lower water concentrations.

* The population estimates presented in Table 3 of the Notice could not be validated. The Notice does not present all of the assumptions used to calculate population sizes. When extremely conservative assumptions are made, calculated population sizes are still much lower than EPA's estimates. For example, if it is assumed that the entire population served by a PWS is exposed to perchlorate at levels above the MRL when at least one sample collected in the PWS contained perchlorate at or above the MRL (even if all other samples did not detect perchlorate) and that the size of the population is the maximum associated with the category assigned to a given PWS (i.e., very small, small, medium, large, very large), the computed maximum exposed population size is approximately 10.5M-this is approximately 60% of EPA's maximum estimate of 16.6M. This lower estimate is still extremely conservative and unlikely to accurately represent the size of the exposed population. The entire population served by the PWS is not likely to be served water from the entry point that had the highest reported concentration, and actual population sizes for each PWS are likely to be distributed across the range of population sizes associated with a given population category. Alternatively, if it is assumed that the population served by a PWS is equally distributed among entry points to the PWS and the total exposed population is computed based only on those entry points where perchlorate was detected above the MRL (i.e., in a manner consistent with the last column of EPA's Table 3), the estimated population size is about half of EPA's 5.1M estimate.

* It appears that EPA included monitoring data for untreated source water in its exposure estimates. Based on the data retrieved from EPA's UCMR1 website, the UCMR1 data includes a total of 34,728 analyses for perchlorate (EPA reports 34,221 analyses), with 647 detections of perchlorate at or above the MRL (EPA reports 637 detects). These detections include 288 detections in source water (out of 10,684 samples, or a frequency of detection of 2.7%) and 348 detections in entry point water (out of 23,319 samples, or 1.5%) (perchlorate was not detected in any samples from the midpoint of distribution systems (n = 16), the point of maximum retention (n = 19), or the location in distribution systems where disinfectant residual is lowest (n = 6); perchlorate was detected in 11 of 684 samples from "unknown" locations). Thus, it is questionable as to whether the number of

people presented in the Notice is likely to drink untreated source water from PWSs, and data from drinking water entry points indicates that concentrations at the entry points are generally lower.

These observations indicate that using the UCMR1 database to extrapolate exposures to concentrations below the MRL would be inappropriate, as it would produce highly inaccurate estimates.

Response: Regarding the comment that UCMR data overestimates current concentrations of perchlorate in drinking water, see response to comment ID 28856 under comment code 3100.

Regarding the comment that perchlorate is not ubiquitous in drinking water but areas of detection appear to be regionalized, UCMR data is the most extensive nationally representative occurrence data for perchlorate in public water systems; therefore, EPA analyzed this data and additional occurrence data in making a regulatory determination for perchlorate as required by Congress. See SDWA Section 1445(g).

Regarding validation of population estimates, see responses to comment IDs 28856 and 28870 under comment code 3100. Also, see "The Analysis Of Occurrence Data from The First Unregulated Contaminant Monitoring Regulation (UCMR 1) In Support Of Regulatory Determinations For The Second Drinking Water Contaminant Candidate List" for a description of how the UCMR 1 population analysis was conducted.

EPA disagrees with the commenter that approximately half of perchlorate water samples in the UCMR 1 database are from untreated source waters. The data EPA used to evaluate perchlorate occurrence from UCMR 1 was only taken from finished water. EPA did allow monitoring at source water sampling points; however, if perchlorate was detected in a source water sample, the UCMR 1 required that follow-up samples be collected at the entry point to the distribution system and follow the monitoring frequency specified in the rule for the contaminant and water source type. A detailed description of UCMR monitoring can be found in the Federal Register under docket number EPA–HQ–OW–2007–0068. The title of the reference that describes UCMR is "The Analysis Of Occurrence Data From The First Unregulated Contaminant Monitoring Regulation (UCMR 1) In Support Of Regulatory Determinations For The Second Drinking Water Contaminant Candidate List."

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28904
EPA Comment Code: 3100

Comment: 3. EPA's proposed analysis of occurrence data is concerning in that the estimated population sizes in the Notice could not be reproduced, the data from UCMR1 are not current and likely overestimate current exposures, and the highest concentration detected anywhere in a PWS was used to estimate exposures for all people served by the PWS, even if the sample was collected from untreated source water or all other samples were nondetects. Altogether, these assumptions

produce an inaccurate and overly conservative estimate of potential human perchlorate exposures from drinking water.

Response: See response to comment IDs 28856 and 28870 under comment code 3100.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 29097
EPA Comment Code: 3100

Comment: EPA assumes that if the drinking water testing at the entry point reports at least one sample above the detection limit during the 2000-2005 UCMR sampling period, the entire population that draws drinking water from that intake is exposed. EPA then multiplies this estimate of the exposed population by an estimate of the proportion of the national population that is pregnant during any given year.

The major overestimate in EPA's calculation concerns the population exposed above the HRL. Under the UCMR regulation, public water systems were required to take multiple samples throughout the year at each sampling point. Large public water systems were required to monitor throughout a three-year period. Many of the sampling points only reported a single detection during the sampling period. Few systems reported perchlorate detections in every sample. Therefore, assuming the total population is exposed at any given time is a gross overestimate. A more likely estimate is the ratio of positive defects to total samples multiplied by the service population.

There are many reasons why a system may have intermittent or a single detection. At the beginning of the UCMR sampling period, laboratory experience with detecting perchlorate was evolving. There have been many anecdotal reports of false detections. Even where perchlorate was found in the drinking water, its occurrence may have been intermittent. Since perchlorate can be naturally formed and then fall to the earth in precipitation, it is likely that watershed concentrations ebb and flow with the natural water cycle.

EPA's estimate in the proposed determination also overestimates the likely number of individuals with drinking water concentrations above the HRL for several other reasons. First, EPA failed to remove individuals who primarily consume bottled water or have in-house treatment systems. EPA did exclude these individuals in its analysis of the UCMR/NHANES data sets.

Second, EPA did not account for system changes in response to the UCMR monitoring. Some states have enacted state-specific drinking water standards. Others have issued advisory levels. Public water systems have responded and have made changes to reduce perchlorate concentrations. These changes are exactly the responses the Safe Drinking Water Act encourages. By prompting local actions, drinking water issues are separated into the local and national concerns. EPA should properly account for these local actions in its population estimate so as to reinforce its finding that exposure does not occur with sufficient frequency to warrant national regulation.

More importantly, EPA should provide the public context for this exposure estimate. Even though there may be potentially exposed individuals above the HRL, the overwhelming scientific evidence

from clinical studies, environmental studies, and from PBPK modeling demonstrates that no one faces an appreciable risk of adverse effect from exposures at EPA's reference dose.

Response: EPA has used the best available data on the frequency and level of perchlorate occurrence in drinking water, the population exposed to perchlorate, and the levels of public health concern to determine that there is a meaningful opportunity for health risk reduction through a national primary drinking water regulation. EPA believes that this analysis is appropriate for making the determination to regulate perchlorate which will initiate a more rigorous health risk reduction, cost analysis, and other analyses required by the Safe Drinking Water Act for proposed drinking water standards. EPA believes that it is appropriate to consider the single highest value reported in a public water system and the highest level within a entry point into the system. While EPA does acknowledge that perchlorate concentrations may fluctuate over time, the duration of life stages where individuals are most sensitive to the effects of perchlorate exposure (i.e., pregnancy and infancy) are relatively short. Therefore EPA believes it is appropriate to use the single highest result from a quarterly or semi-annual sample to determine if these populations are exposed at levels of health concern.

EPA does not believe that multiplying the ratio of positive detects to total samples by the service population is appropriate because this approach would not account for the fact that during certain periods of time the whole population was potentially exposed to perchlorate in drinking water at levels of health concern. EPA does not believe that is appropriate to remove persons who use in house treatment or consume bottled water for these estimates of population potentially exposed. The bottled water consumption and in house treatment data were available for NHANES participants but are not collected or reported under the UCMR. EPA believes that a more rigorous evaluation of the variation in drinking water consumption can be made as part of the health risk reduction and cost analyses required under SDWA for proposed national primary drinking water regulations.

EPA does not believe that it is appropriate to adjust estimates of perchlorate occurrence from those measured under UCMR. EPA believes that the UCMR is the best available data on the frequency and level of perchlorate occurrence in public water systems nationally. EPA acknowledges that levels of perchlorate may have decreased in some public water systems as a result of state regulation or of water system decisions. However, those may also be instances in which levels of perchlorate may have increased due to new contamination. EPA further notes that public water systems would conduct monitoring under the national primary drinking water regulation we expect to promulgate. Systems which do not detect perchlorate at levels exceeding the MCL will not be required to take action to lower perchlorae levels. Therefore if systems have already taken actions to address perchlorate in their drinking water, these systems may not have to take any further steps to remove perchlorate .

Regarding the statement that no one faces an appreciable risk of adverse effects from exposures at EPA's reference dose, a recent study (Steinmaus et al., 2010) examining the perchlorate concentration in drinking water and its association with neonatal thyroid hormone levels in over 400,000 newborns, concluded that there is a statistically significant association with perchlorate exposure and increased neonatal thyroid hormone levels. This study has shown that, at environmental concentrations of perchlorate greater than 5 ug/L, the odds of elevation in thyroid stimulating hormone (TSH) levels at birth was significantly greater, when compared to hormone levels in newborns from communities unexposed to perchlorate. Steinmaus et al. (2010) grouped

geographic communities in California according to whether their respective estimated average perchlorate concentrations were either more or less than 5 ug/L, therefore, unexposed communities in this particular study were defined as having less than 5 ug/L drinking water perchlorate concentrations (representing an average estimate of perchlorate concentrations of the different water systems supplying a given community, and weighted by the number of water sources used by each system). Therefore, for the Steinmaus et al. (2010) study, this particular unexposed group includes communities with estimated average perchlorate concentrations of 5 µg/L or less, as well as all communities with no measurable environmental perchlorate concentrations. The U.S. EPA reference dose for perchlorate is 0.7 ug/kg/day. EPA has adopted the NRC's recommendations regarding the reference dose for perchlorate in its "Integrated Risk Information System" (IRIS) (USEPA 2005), resulting in an RfD of 0.7 ug/kg/day, which was derived by applying a 10-fold (10x) uncertainty factor to the NOEL of 7.0 ug/kg/day.

EPA Comment Code: 3120 UCMR 1 statistical methodology and nationally representative sample of small systems

Individual Comments
Commenter Name: Melanie A. Marty, Ph.D.
Commenter Organization: Children's Health Protection Advisory Committee
EPA Document ID: EPA-HQ-OW-2008-0692-0962
EPA Comment ID: 20420
EPA Comment Code: 3120

Comment: The other concern is that, as noted earlier, without a federal MCL, detections of high level contamination (e.g., 1300 ug/L of perchlorate in a public water supply in Boxborough MA) will go undetected leading to high localized exposures. This high level of contamination would not have been detected without a state initiated testing program (MADEP, 2005). Given the unpredictable nature of these extreme concentrations, national monitoring is clearly needed.

The 2001 Unregulated Contaminant Monitoring Regulation (UCMR) for perchlorate focused upon larger public water supplies and is not indicative of the numbers of people exposed or extent of exceedances possible from localized hot spots due to contamination of water from blasting, fireworks or industrial/military releases.

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120. EPA intends to consider compliance monitoring requirements and request comment as part of the expected proposed national primary drinking water regulation for perchlorate. EPA disagrees with the statement that the UCMR is not indicative of the numbers of people exposed to perchlorate. Under UCMR 1, EPA collected samples from all the large PWS (3,865) and 800 small PWS which were a stratified random sample of public water systesms selected to represent drinking water occurrence nationally. EPA has determined that UCMR 1 is the best available scientific perchlorate occurrence data collected in accordance with acceptable analytical methods. EPA's determination is based upon the fact that UCMR1 is the most nationally representative study of the frequency and levels of perchlorate in drinking water systems.

Commenter Name: Ron Curry
Commenter Organization: New Mexico Environment Department
EPA Document ID: EPA-HQ-OW-2008-0692-1796
EPA Comment ID: 20932
EPA Comment Code: 3120

Comment: Because perchlorate is not currently regulated under the SDWA, data on perchlorate contamination in New Mexico public water systems is limited. Under the Unregulated Contaminant Monitoring Rule,[FN1: 40 C.F.R. [section] 141.40.] public water systems serving communities of greater than 10,000 persons were required to monitor for perchlorate for one year between 2001 and 2003. A "statistically representative" number of additional smaller systems were also required to monitor for perchlorate for one year during this time period. However, with few exceptions, that monitoring data does not appear to have been reported to the State of New Mexico. Therefore, the

Environment Department has only a very incomplete picture of perchlorate contamination in public water systems in the State.

Response: EPA has made the UCMR monitoring data publicly available. EPA has determined that this data is the best available data (collected in accordance with accepted methods) on the occurrence of perchlorate nationally.

EPA Comment Code: 3140 UCMR 1 entry-point-level estimation of perchlorate exposure

Individual Comments
Commenter Name: Caroline Baier-Anderson, PhD
Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20952
EPA Comment Code: 3140

Comment: Perchlorate is Present at Sufficient Levels and Frequency to Constitute a Public Health Concern

EPA's determination of whether perchlorate is present at sufficient levels and frequency to constitute a public health concern begins with an analysis of occurrence and population estimates for perchlorate at various thresholds. Since the data on occurrence may not represent water samples delivered to the entire service population, EPA considers two values fore each threshold or cut-point considered (e.g., 4, 5, 7, 10, 12, 15, 17, 20 and 25 ug/L); the first value is the service population, and the second is an estimate below the service population, that is derived from the service population divided by the number of entry or sample points. The second value is in all cases substantially lower than that of the service population. To ensure the protection of public health, we recommend that the more conservative number - that of the entire service population - should be considered as the potentially impacted population.

Response: EPA has decided to regulate perchlorate in drinking water. See response to comment code 6120. In the Federal Register notice "Final Regulatory Determination on Perchlorate" EPA considers a range of estimates of the population served by PWSs that had at least one sample with perchlorate concentrations greater than the potential HRLs. The population range represents both a high end estimate, as well as a central value estimate. The high end estimate is derived by adding the entire system population of all PWSs in which at least one sample was found to contain perchlorate above thethreshold. EPA considers this a high end estimate because it is based on the assumption that the entire system population is served water from the entry point that had the highest reported perchlorate concentration. In fact, many PWSs have multiple entry points into which treated water is pumped for distribution to their consumers. For the PWSs with multiple entry points, it is unlikely that the entire service population receives water from the one entry point with the highest single concentration. Therefore, EPA also provides a central value estimate of the population served water with perchlorate above a threshold. EPA developed this central value estimate by assuming the population was equally distributed among all entry points and added only the proportion of the total population served by those entry points in a PWS that had at least one sample with perchlorate concentrations greater than the threshold. EPA considered both the high end estimate and central value estimate in making this final regulatory determination. The Agency considered the central value estimate as well because this is likely a better estimate of the population exposed to perchlorate at levels of public health concern.

Commenter Name: Shannon Cunniff
Commenter Organization: Department of Defense (DOD)

EPA Document ID: EPA-HQ-OW-2009-0297-0411
EPA Comment ID: 28525
EPA Comment Code: 3140

Comment: Comment No. 14

Section III. B. 3. Alternative Approaches for Calculating HRLs

Page & Paragraph Page 41889 Table 3

Comment Example of comment # 2: In the use of the UCMR 1 data, the EPA indicates that an adjustment was made for water systems with multiple entry points to decrease the estimated population exposed to the "threshold of interest." However, in reviewing the outcome of this analysis (Table 3, EPA 2009), the reviewer is unable to readily duplicate the adjusted population estimates provided.

Suggested Action, Revision and References (if necessary) The Table 3 values need to be reviewed and insured to be readily duplicable by external reviewers.

Category* E

Response: A more detailed description of the methodology for conducting a proportional population analysis of UCMR 1 data, such as the analysis used to derive the population estimates for entry or sample points having at least one detection greater than the threshold of interest in column five of Table 3 of the August 2009 FR Notice, can be found in the document titled "The Analysis Of Occurrence Data From The First Unregulated Contaminant Monitoring Regulation (UCMR 1) In Support Of Regulatory Determinations For The Second Drinking Water Contaminant Candidate List" in docket number EPA–HQ–OW–2007–0068. Please refer to the Proportional Populations Section of this document under Section 4.3 "Sample-Point-Level Analyses".

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection (MassDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0495
EPA Comment ID: 28866
EPA Comment Code: 3140

Comment: We also wish to note that the population estimates in column 5 of Table three would be likely to underestimate those exposed in MA, and quite likely other states, due to mixing of supplies from multiple entry points.

Response: Please see the response to comment ID 20952 in comment code 3140. In addition to the central value population estimates provided in the "Final Regulatory Determination on Perchlorate" notice, EPA also considered estimates of the total population served by drinking water systems in which at least one sample was found to contain perchlorate above the threshold (i.e., the high end estimate) to account for the mixing of supplies from multiple entry points to the distribution system.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group (EWG)

EPA Document ID: EPA-HQ-OW-2009-0297-0499
EPA Comment ID: 28933
EPA Comment Code: 3140

Comment: Occurrence analysis: EPA's occurrence analysis grossly underestimates the number of people at risk from perchlorate because of an inappropriately high detection and reporting threshold of four ppb.

In table 3 of the notice in the federal register, the Agency lists the occurrence and population estimates for perchlorate above a number of thresholds, starting at 4ppb. This data is derived from the Agency's Unregulated Contaminant Monitoring Rule (UCMR) 1; the Agency estimates that a total of 16.6 million people in the United States are served by public water systems with at least 1 detection of perchlorate at > 4 ppb.

In table 2 of the federal register, the agency finds that HRLs as low as 1 are necessary to prevent children ages two and younger who have higher water ingestion rates and cumulative perchlorate exposures that can easily exceed the RfD. In addition, as mentioned above, the degree of perchlorate contamination of some powdered infant formulas is so high than an HRL as low as 0 is justified for infants six months and younger. Therefore, the finding of perchlorate in drinking water at any level presents risks to vulnerable populations and until the minimum reporting level (MRL) is decreased to reflect this, the agency's numbers are an underestimate.

Response: EPA acknowledges that there are newer and more sensitive analytical methods that are now available that would permit perchlorate analysis with reporting limits below 4 ug/L (the MRL for perchlorate under the UCMR 1 was 4 ug/L); however, the 1996 amendments to the Safe Drinking Water Act require the Agency to consider the best available, peer reviewed science when developing drinking water standards. In applying these principles, "best available" usually refers to the availability at the time an assessment is made. EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). As part of the rulemaking process, EPA plans further analyze perchlorate occurrence data to estimate the additional number of PWSs and entry points and the population served at levels of public health concern.

EPA Comment Code: 3150 Potential use of a Bayesian model to estimate number of PWSs and population served at a range of thresholds

Response to Code 3150: EPA continues to evaluate the utility of the Bayesian model(s) in the development of a NPDWR for perchlorate. EPA plans to be transparent in explaining the analysis and any assumptions made when presenting the analysis in connection with the proposed NPDWR. EPA does not intend to distinguish the source of perchlorate in drinking water but does intend to assess the number of water systems impacted by a potential regulation.

Individual Comments
Commenter Name: James D. Taft
Commenter Organization: Association of State Drinking Water Administrators
EPA Document ID: EPA-HQ-OW-2009-0297-0525
EPA Comment ID: 28500
EPA Comment Code: 3150

Comment: a. EPA requests comment on the potential use of a Bayesian model to estimate the number of public water systems, and populations served by such systems, with at least one estimated sample detection greater than 1, 2, 3, 4, 5, 7, 10, 12, 15, 17, 20, and 25 [mu]g/L.

ASDWA feels that it is necessary to do further modeling to estimate perchlorate levels below the analytical method MRL used in the UCMR monitoring and the Baysean modeling approach discussed in the notice strikes us as a reasonable one. Data from Massachusetts with a lower detection limit can be used to refine and validate the modeling so that more precise estimates can be made of occurrence at these very low levels. EPA should also include any new data received as a result of this notice in its analysis.

Response: See response to comment code 3150. EPA has reviewed other occurrence data.

Commenter Name: Kay Brothers
Commenter Organization: Southern Nevada Water Authority
EPA Document ID: EPA-HQ-OW-2009-0297-0667
EPA Comment ID: 28694
EPA Comment Code: 3150

Comment: September 17, 2009

Water Docket Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Ave., NW Washington, DC 20460

SUBJECT: Comments on the Drinking Water: Perchlorate Supplemental request for Comments Docket ID No. EPA-HQ-OW-2009-0297

The Southern Nevada Water Authority (Authority) appreciates the opportunity to comment on the preliminary regulatory determination for perchlorate as listed in the August 19, 2009 Federal Register (74 FR 41883). The Authority is a cooperative agency formed in 1991 to address Southern

Nevada's unique water needs on a regional basis. Officials of the Authority are charged with managing the region's water resources and providing for approximately 2 million area residents' present and future water needs. The Authority is governed by a seven- member board comprised of representatives from each of its member agencies, which include the cities of Boulder City, Henderson, Las Vegas and North Las Vegas, as well as agencies serving customers in unincorporated Clark County and the town of Laughlin.

The Authority's responsibilities include managing water supplies available to Southern Nevada and regional conservation programs as well as building and operating regional facilities to provide a reliable drinking water delivery system to all member agencies.

Interpretation of the Physiologically-Based Pharmacokinetic (PBPK) Modeling

The Authority strongly encourages the use of sound science in the consideration of federal regulation of perchlorate. While modeling such as the PBPK and Bayesian hierarchical models suggested in the noted Federal Register (FR) are of value when empirical data are unavailable, the use of these models for the elucidation of health reference levels and national occurrence, respectively, are not necessary as sufficient data already exist.

Response: EPA continues to evaluate the utility of the Bayesian model(s) in the development of a NPDWR for perchlorate. EPA plans to be transparent in explaining the analysis and any assumptions made when presenting the analysis in connection with the proposed NPDWR. See response to comment code 3150.

Commenter Name: Kay Brothers
Commenter Organization: Southern Nevada Water Authority
EPA Document ID: EPA-HQ-OW-2009-0297-0667
EPA Comment ID: 28698
EPA Comment Code: 3150

Comment: Occurrence Analysis

The Authority also does not support the use of Bayesian hierarchical models to extrapolate the Massachusetts' occurrence data to develop a portrait of sub-4 ug/L perchlorate occurrence nationwide. While we understand the great value of Bayesian models, we see no reason for applying these models considering that the preponderance of data suggest that perchlorate is not relevant to human health even at 4 ug/L and considering the inappropriateness of applying a relative source contribution (RSC) factor to perchlorate when using the Greer study or others where dietary contributions have already been accounted. Moreover, other studies have already shown that perchlorate is ubiquitous in the environment at concentrations above approximately 0.050 ng/L (Rickman 2003; Richardson 2004; Snyder, Vanderford et al. 2005), owing largely to the atmospheric formation and subsequent deposition of perchlorate in rain (Dasgupta, Martinelango et al. 2005; Rajagopalan, Anderson et al. 2006).

Response: See response to comment code 3150. EPA disagrees with the commenter's view that perchlorate is not relevant to human health even at 4 ug/L and that applying an RSC factor to perchlorate is inappropriate. See response to comment code 5220 for an explanation of EPA's

rationale in concluding that perchlorate is relevant to human health at or below 4 ug/L. See response to comment code 5210 for an explanation of EPA's use of an RSC.

Commenter Name: Mic Stewart
Commenter Organization: Water Quality Section, Metropolitan Water District of Southern California
EPA Document ID: EPA-HQ-OW-2009-0297-0496
EPA Comment ID: 28712
EPA Comment Code: 3150

Comment: Additional Comments on Occurrence Analysis and Potential Use of a Bayesian Model

EPA has requested comments on the appropriateness of its exposure model to estimate the number of public water systems and populations served by such systems. The American Water Works Association and other water industry associations have suggested that the use of Bayesian modeling is not necessary to support the Agency's regulatory decision-making for perchlorate. Metropolitan suggests that any methodology employed by EPA to interpret occurrence data be consistent with other established methods used with other regulatory development.

Response: EPA continues to evaluate the utility of the Bayesian model(s) in the development of a NPDWR for perchlorate. EPA plans to be transparent in explaining the analysis and any assumptions made when presenting the analysis in connection with the proposed NPDWR. See response to comment code 3150.

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 28746
EPA Comment Code: 3150

Comment: 3. Use of a Bayesian model for the purposes stated in the August 19, 2009 Federal Register requires additional justification as it will lead to an overestimation of the low-level occurrence of perchlorate if calibrated to select geographical areas and/or small data sets.

Response: See response to comment code 3150.

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 28753
EPA Comment Code: 3150

Comment: C. Occurrence Analysis 4. Request for Comment on Alternative Approaches a. EPA requests continent on the potential use of a Bayesian model to estimate the number of public water systems, and populations served by such systems, with at least one estimated sample detection greater than 1, 2, 3, 4, 5, 7, 10, 12, 15, 17, 20, and 25 ug/L.

Comment C.4.a.1: Use of a Bayesian model for the stated purpose is not recommended nor supported by the NDEP. The NDEP understands that the national occurrence data for perchlorate were generated between 2001 and 2005. Further, we understand that EPA Method 314 was used for analysis of the occurrence data. The typical reporting limit associated with EPA Method 314 is 4 ug/L. EPA required the collection and submittal of the national occurrence data knowing this limitation.

It is not clear how use of a Bayesian model now for revaluating the existing occurrence data could be considered as a reasonably defensible approach for analysis. This is because it likely will lead to an overestimation of the low- level occurrence of perchlorate if calibrated to select geographical areas and/or small data sets.

Response: See response to comment code 3150.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28808
EPA Comment Code: 3150

Comment: REQUEST FOR COMMENT ON ALTERNATIVE APPROACHES

a. On the use of a Baysian model to estimate number of public water systems.

NRDC response: NRDC has no opinion on this.

Response: No response necessary

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28837
EPA Comment Code: 3150

Comment: 74 FR 41891: "EPA requests comment on the potential use of a Bayesian model to estimate the number of public water systems and populations served by such systems, with at least one estimated sample detection greater than 1, 2, 3, 4 ug/l, etc."

The Bayesian extrapolation of UCMR1 occurrence data is a complex analysis and therefore EPA needs to be transparent in explaining the analysis in its final regulatory determination. AMWA requests that EPA also clearly state the assumptions of the modeling effort. AMWA recommends that the effort recognize that the data available shows that perchlorate occurrence is not evenly distributed across the country.

Response: EPA continues to evaluate the utility of the Bayesian model(s) in the development of a NPDWR for perchlorate. EPA plans to be transparent in explaining the analysis and any assumptions made when presenting the analysis in connection with the proposed NPDWR. See response to comment code 3150.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0415
EPA Comment ID: 28853
EPA Comment Code: 3150

Comment: Occurrence Analysis

The Agency requested comments on the appropriateness of using a Bayesian model to estimate perchlorate occurrence in public water systems and populations served by such systems. This estimate would use UCMR1 data that had a laboratory detection level of 4 ug/L and project national occurrence at levels below 4 ug/L. While AWWA recognizes the validity of Bayesian modeling, we believe that the study as proposed is not necessary to support the Agency's regulatory decision making for perchlorate. The weight of evidence as discussed in our comments does not support the need for further analysis of occurrence since regulation of perchlorate would not present a meaningful opportunity for health risk reduction for persons served by public water systems.

Response: The Agency has concluded that there is a meaningful opportunity for health risk reduction for persons served by public water systems through a National Primary Drinking Water Rule for perchlorate. EPA acknowledges that the use of Bayesian modeling is not necessary for making a regulatory determination on perchlorate. EPA continues to evaluate the utility of the Bayesian model(s) in the development of a NPDWR for perchlorate.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0415
EPA Comment ID: 28854
EPA Comment Code: 3150

Comment: Multiple studies have presented data demonstrating that perchlorate is widely found at low levels and may originate from anthropogenic and/or natural sources; it even occurs in some dietary supplements [FN14: Snyder, S., Pleus, R., Vanderford, B., J. Holady. 2006. Perchlorate and chlorate in dietary supplements and flavor enhancing ingredients. Analytica Chimica Acta, 567:1:26.] and groundwater more than 28,000 years old [FN15: Plummer, L. N.; Bohlke, J. K.; Doughten, M. W. 2006. Perchlorate in pleistocene and holocene groundwater in North-Central New Mexico. Environ. Sci. Technol. 40:1757.]. Since the major route of exposure is food and not water, estimating low level concentrations of perchlorate in the minor source will not provide any additional useful information. The only reason to determine perchlorate concentrations in water is to estimate human exposure. Given the previous discussion and the Agency's assessments, there clearly is sufficient data from human studies that have been completed to sufficiently characterize exposure. These studies (e.g. NHANES, FDA Total Diet Study) examined urine, saliva, and breast milk and in all cases the study subjects had perchlorate. There were no studied individuals who did not have perchlorate. So we know that in the U.S., exposure to perchlorate is very close to universal. Further, examination [FN16: Brandbuber , P, Clark, S. and K. Morley. (publication pending) The Occurrence of Perchlorate in Public Drinking Water Systems, Journal AWWA.] of the existing UMCR dataset provides no general indicator of a causal relationship between occurrence and known locations of perchlorate releases with exception of locations at extremely high levels that were typically adjacent

to industrial and military users of perchlorate. In the vast majority of UCMR occurrences, an obvious source could not be easily identified. Studies [FN17: Jackson, W., Rainwater, K., Anderson, T., Lehman, T., Tock, R., Rajagopalan, S., and M. Ridley. 2004. Distribution And Potential Sources Of Perchlorate In The High Plains Region Of Texas Final Report. Submitted to the Texas Commission on Environmental Quality.],[FN18: Duncan, P.B, Morris, R.D., and E. Vavricka. 2005. Forensic identification of anthropogenic and naturally occurring source of perchlorate. Environmental Forensics, 6:205-215.],[FN19: Dasgupta, P., Martinelango, P., Jackson, W., Anderson, T., Tian, K., and R. Tock. 2005. The Origin of Naturally Occurring Perchlorate: The Role of Atmospheric Processes Environ. Sci. Technol., 39:6:1569 -1575.],[FN20: Balaji Rao, Todd A. Anderson, Greta J. Orris, Ken A. Rainwater,* Srinath Rajagopalan, Renee M. Sandvig, Bridget R. Scanlon, David A. Stonestrom, Michelle A. Walvoord, and W. Andrew Jackson (2007) Widespread Natural Perchlorate in Unsaturated Zones of the Southwest United States Environ. Sci. Technol, 41:4522-4528.] of natural occurrence also do not provide a sound basis for predicting occurrence of perchlorate, unlike other inorganic substances that may associate with specific geological formations such as radionuclides and arsenic.

The Agency has proposed a statistical Bayesian procedure to estimate the distribution of censored perchlorate data. There are several different such procedures (Maximum Likelihood Estimate, Kaplan-Meier Non-Parametric techniques, Regression on Order Statistics) however that all make assumptions about the nature of the distribution, whether normal, log-normal, or non-normal. The Agency has not explained why this particular model would be used versus one of the other approaches noted here. Nor does the Agency explain what population distribution is being assumed. Without this information, it is impossible to comment on the validity of the proposed procedures for this or potentially future applications of this approach. Regardless, all such procedures must assume that a single population of results is being estimated. However there appear to be multiple populations of results, those resulting from natural sources, munitions, Chilean fertilizers, etc. There may, of course, be more than one natural source as cited in the studies previously noted. Given the fact that the occurrence data is mostly poly-modal due to multiple sources in areas such as California and Massachusetts, the use of any statistical procedure that is based on a mono-modal distribution will have little likelihood of producing useful results.

Response: See response to comment code 3150.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection (MassDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0495
EPA Comment ID: 28865
EPA Comment Code: 3150

Comment: Section III C: Occurrence Analysis

4(a)) EPA's proposal to use a Bayesian model to estimate the number of public water systems, and populations served by such systems, with sample detections at various levels appears to be a reasonable approach. Further details regarding the specific model inputs are, however, needed in order to assess the usefulness of the model. MassDEP will provide U.S. EPA with Massachusetts perchlorate monitoring data to assist in this effort. However, we wish to note that the sampling results and data distribution for MA may not reflect the situation in other states.

Response: EPA appreciates MassDEP's offer to provide EPA with Massachusetts perchlorate monitoring data and acknowledges that MA's sampling results and data distribution may not be representative of other states. See response to comment code 3150.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28891
EPA Comment Code: 3150

Comment: 1. EPA requests comment on the potential use of a Bayesian model to estimate the number of public water systems, and the population served by such systems, with at least one estimated sample detection greater than 1, 2, 3, 4, 5, 7, 10, 12, 15, 17, 20, and 25 ug/L.

With regard to perchlorate's regulatory determination, extrapolating the frequency of occurrence of perchlorate in U.S. drinking water at concentrations less than the MRL of 4 ug/L is unnecessary because scientific data provide no evidence that adverse health effects can occur at these levels. Data for average adults (e.g., Greer et al., 2002) suggest that IUI at water concentrations less than 245 ppb (the drinking water equivalent of the POD) would be statistically insignificant, and the Notice suggests, based on EPA's PBPK model for several life stages, that IUI at water concentrations corresponding to the RfD (i.e., 24.5 ppb) would be less than 2%.

Further, UCMR1 data are insufficient for estimating population sizes exposed to concentrations greater than the MRL of 4 ug/L, and therefore may not be used to reliably estimate exposures below the MRL. As elaborated below, examination of EPA's occurrence analysis is made difficult by the fact that the Notice lacks the required transparency concerning the assumptions it used to calculate sizes of populations potentially exposed to different threshold concentrations (Table 3, U.S. EPA, 2009b). The Notice's summary of the UCMR1 data likely overestimates current exposure concentrations and the number of people exposed to perchlorate above various threshold levels.

Response: See response to comment code 3150. See response to comment code 5220 for an explanation of EPA's rationale in concluding that adverse health effects occur at levels below 24.5 ppb. EPA believes that UCMR1 data are sufficient for estimating population sizes exposed to concentrations greater than the MRL of 4 ug/L. See response to comment ID 28525 under comment code 3140 for an explanation of the EPA's population analysis of UCMR 1 data.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Department of Environmental Protection (NJDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0527
EPA Comment ID: 28913
EPA Comment Code: 3150

Comment: We support the use of Bayesian statistical models and approaches to estimate the occurrence of perchlorate in public water systems and the number of people exposed at concentrations below the minimum reporting level (MRL) in the occurrence studies on which the analysis is based. **Response:** See response to comment code 3150.

Commenter Name: Danielle Blacet

Commenter Organization: Association of California Water Agencies
EPA Document ID: EPA-HQ-OW-2009-0297-0208
EPA Comment ID: 28925
EPA Comment Code: 3150

Comment: 3) Potential use of Bayesian model (page 41891)

ACWA feels that the Bayesian model would not be useful for the purposes of this determination as we already know that at low enough concentrations perchlorate is widely found, if not ubiquitous. Dr. Shane Snyder and others have completed research that indicates perchlorate exists in basically every water source studied and that US exposure to perchlorate is very close to universal. Several human exposure studies (e.g. NHANES) have also looked at urine, saliva, and breast milk and every single study subject in each study had perchlorate--there were no studied individuals who did not have perchlorate. Estimating this data is not necessary when real data is already available.

In addition, since the major route of exposure is food and not water, estimating low level concentrations of perchlorate in the minor source will not provide any additional useful information to determine if this chemical needs to be regulated.

Further, while the USEPA is proposing to use a statistical Bayesian procedure to estimate the distribution of censored perchlorate data, it has not been explained why this particular model would be used and not some other model nor do they explain what population distribution is being assumed. However, all such procedures must assume a single population of results being estimated. In the case of perchlorate, there appear to be multiple populations of results, those resulting from potentially several distinct natural sources, munitions, and Chilean fertilizers. Given the fact that the data should be poly-modal due to these multiple sources found in areas such as California and Massachusetts, the use of any statistical procedure that is based on a mono-modal distribution will have little likelihood of producing useful results.

Again, ACWA appreciates the opportunity to submit comments on this critical determination, and USEPAâ€™s efforts to protect public health through the provisions of the federal Safe Drinking Water Act. We trust USEPA will consider all of the good science that is available when making a final regulatory determination.

If you have any questions, please feel free to call our offices at 916-441-4545 or 202-434- 4760.

Sincerely,

Danielle Blacet Regulatory Advocate

Abby Schneider, Ph.D. Federal Legislative Representative

Response: EPA did not use the Bayesian model to make the regulatory determination on perchlorate. EPA continues to evaluate the utility of the Bayesian model(s) in the development of a NPDWR for perchlorate. EPA may not necessarily distinguish the source of perchlorate in drinking water but does intend to assess the number of water systems impacted by a potential regulation.

EPA Comment Code: 3160 Use of Census data to estimate populations that are in the sensitive life stage

Individual Comments
Commenter Name: James D. Taft
Commenter Organization: Association of State Drinking Water Administrators
EPA Document ID: EPA-HQ-OW-2009-0297-0525
EPA Comment ID: 28501
EPA Comment Code: 3160

Comment: b. EPA requests comment on using U.S. Census data to estimate the portions of the population that are in the sensitive life stage at any one time.

US Census data are appropriate to estimate the population numbers for subpopulations that may be more vulnerable to perchlorate. As mentioned above, if sensitive subpopulations are going to be considered when making the regulatory determination, accurate estimates of how many people will be protected are critical to the decision.

Response: Please see the response to comment ID 28809 in comment code 3160.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28809
EPA Comment Code: 3160

Comment: b. On the use of US Census data to estimate portions of the population that are in the sensitive life stage at any one time

NRDC response: Yes, the U.S. Census data is appropriate for this use.

Yes, EPA should use the U.S. census data. The U.S. census is mandated by the U.S. Constitution, and is conducted every 10 years, with the next one planned for 2010. These data are used by Congress, as well as governments at the local, state, and tribal level to make important decisions about setting priorities, providing services, disbursing funds, and even distributing Congressional seats.[FN62: See e.g. http://2010.census.gov/2010census/] The census data are widely recognized to be reliable, credible, and useful.

There is a valid concern that these data under-represent certain populations, such as certain ethnic minorities, who may be "unregistered" for census purposes. This may be relevant to the use of these data for this perchlorate assessment, because the children of ethnic minorities may not be fully represented. If anything, these data would underestimate the number of children under 1 year old.

Response: Please see response to comment ID 28867 under comment code 3160. EPA will further take into consideration the effect contaminants have on subgroups that comprise a meaningful portion of the general population (such as infants, children, pregnant women, the elderly, and

individuals with a history of serious illness) as we develop the proposed NPDWR, as required by Section 1412(b)(1) of the Safe Drinking Water Act.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection (MassDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0495
EPA Comment ID: 28867
EPA Comment Code: 3160

Comment: 4(b)) EPA requested comments on using US Census data to estimate the portions of the population that are sensitive at any one time to perchlorate in drinking water. This analysis is used as one factor in EPA's decision-making on the need for a drinking water standard for perchlorate, based on the number of people in the U.S. who would be at risk. MassDEP believes that it is inappropriate to consider sensitive groups one-by-one using census or any other data. EPA should certainly consider perchlorate exposures to fetuses, infants and young children up to 2 years of age. However, EPA should also, for several reasons, consider the entire population's exposure. First, Blount et al. (2006) and Steinmaus et al. (2007) reported an association between perchlorate exposure and decreased T4 and increased TSH in iodine deficient adult women and increased TSH in all women. As such, we believe that all women should be included in EPA's analysis as a sensitive subgroup. Secondly, as previously noted, there are other sensitive members of the population beyond fetuses, infants and women, and they should also be factored into EPA's framework for considering the extent of the population at risk to perchlorate exposures from drinking water. Lastly, because significant exposures to other thyroid toxicants are known to occur, other members of the population may also be at increased risk. Thus, any estimate derived based on exposures to the fetus, neonate and women as a group will still be an underestimate of those actually at risk.

We appreciate the opportunity to comment. For further information please contact Carol Rowan West at 617-292-5510 (Carol.RowanWest@state.ma.us), C. Mark Smith at 617-292-5509 (C.Mark.Smith@state.ma.us) or Tsedash Zewdie at (617) 292-5842 (Tsedash.Zewdie@state.ma.us).

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Response: EPA considered the population estimates served by PWSs that were monitored under UCMR 1 for which the highest reported perchlorate concentration was greater than various threshold concentrations when determining that a regulation for perchlorate was warranted. These population estimates are for people at all life stages. EPA has determined that a NPDWR for perchlorate could reduce perchlorate exposures for these populations to levels below the potential alternative HRLs that EPA has identified as levels of public health concerns for purposes of this determination, and that such exposure reductions present a meaningful opportunity for the reduction of health risks for persons served by PWSs. Please see the final regulatory determination notice for further discussion of this analysis.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28893
EPA Comment Code: 3160

Comment: 2. EPA requests comment on using U.S. Census data to estimate the portions of the population that are in the sensitive life stage at any one time.

U.S. Census data might be useful if PWS data are paired with U.S. Census data for the same locations. As discussed above, the relevance of the UCMR1 data to current exposure is unclear since the UCMR1 data, which were collected from 2001 to 2005, likely overestimate current concentrations, and approximately half of the perchlorate water samples in the UCMR1 database are from untreated source waters. Evaluating perchlorate in drinking water at low concentrations (e.g., less than the concentration corresponding to the RfD of 24.5 ppb) is unnecessary as no adverse health effects are expected at these levels.

Response:
Please see response to comment ID 28809 under comment code 3160.

EPA acknowledges that there may be sources that had detected perchlorate from UCMR1 monitoring that are either no longer being used or are being treated per the requirements of maximum contaminant levels established in California and Massachusetts; however, the 1996 amendments to the Safe Drinking Water Act require the Agency to consider the best available, peer reviewed science when developing drinking water standards. In applying these principles, "best available" usually refers to the availability at the time an assessment is made. UCMR data is the most

extensive nationally representative occurrence data for perchlorate in public water systems; therefore, EPA analyzed this data and additional occurrence data in making a regulatory determination for perchlorate as required by SDWA Section 1445.

EPA disagrees with the commenter that approximately half of perchlorate water samples in the UCMR 1 database are from untreated source waters. The data EPA used to evaluate perchlorate occurrence from UCMR1 was only taken from finished water. EPA did allow monitoring at source water sampling points; however, if perchlorate was detected in a source water sample, the UCMR 1 required that follow-up samples be collected at the entry point to the distribution system and follow the monitoring frequency specified in the rule for the contaminant and water source type.

EPA disagrees that evaluating perchlorate in drinking water at low concentrations (e.g., less than the concentration of 24.5 ppb) is unnecessary. Since the NRC also identified infants and developing children as additional life stages, EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 µg/L to 47 µg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. EPA is evaluating these potential alternative HRLs and considers them to be levels of public health concern for purposes of this determination. For further discussion of this issue please see today's notice.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Department of Environmental Protection (NJDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0527
EPA Comment ID: 28914
EPA Comment Code: 3160

Comment: We also support the use of U.S. Census data to estimate the numbers of pregnant women, infants, and children.

Response: Please see the response to comment ID 28809 in comment code 3160.

EPA Comment Code: 3170 Accounting for variation of perchlorate levels in public water systems over time

Response to Code 3170: EPA has decided to regulate perchlorate in drinking water. See response to comment code 6120. EPA notes that systems or entry/sample points with at least one detect above the threshold may not expose the population to this level at all times. At any particular time, perchlorate levels may be lower or higher than the highest estimated sample detection. However, EPA believes that estimating the number of systems, entry points and populations with at least one detection above the various threshold concentrations identified in the final perchlorate regulatory determination notice is appropriate for the perchlorate regulatory determination because a single quarterly or semi-annual sample more closely reflects the short term exposure during the life stages identified by the NRC (i.e., fetuses, pre-term newborns, infants and young children) than does the estimated mean concentration of perchlorate at a system.

Individual Comments
Commenter Name: James D. Taft
Commenter Organization: Association of State Drinking Water Administrators
EPA Document ID: EPA-HQ-OW-2009-0297-0525
EPA Comment ID: 28502
EPA Comment Code: 3170

Comment: c. EPA requests comment on how the Agency should account for the variation of perchlorate levels over time in public water systems. EPA believes that estimating the number of systems, entry points and populations with at least one detection above the HRL is appropriate for the perchlorate regulatory determination because a single quarterly or semi- annual sample more closely reflects the short term exposure during life stages of concern (i.e., fetuses, pre-term newborns, infants and young children). However, EPA requests comment on whether the Agency should consider other approaches such as estimating the number of systems, entry points and populations with two or more detections above HRL or some other approach.

ASDWA agrees with EPA's premise that a single occurrence above the HRL could indicate a cause for concern about health impacts due to short term exposure, if the value is not an anomaly. However, on the other hand, a single value above the HRL, especially if the HRL is 15 ug/l or almost 4 times the MRL, that is not supported by additional detections in other samples, could be questionable and indicative of a sampling or laboratory error. EPA should consider an analysis that considers a single sample above the HRL, but with additional detects, as the occurrence criteria. This considers the impact of short term possible health impacts but would tend to eliminate outliers.

Response: See response to comment code 3170. EPA intends to present the perchlorate occurrence analysis that is used to develop the NPWDR.

Commenter Name: Kathy Dolan
Commenter Organization: Food and Water Watch (FWW)
EPA Document ID: EPA-HQ-OW-2009-0297-0526
EPA Comment ID: 28611
EPA Comment Code: 3170

Comment: You also request comment on how the Agency should account for variation of perchlorate levels over time in public water systems. This is simple: the Agency should act with extreme precaution.

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #11 - Food and Water Watch
EPA Document ID: EPA-HQ-OW-2009-0297-0526
EPA Comment ID: 28617
EPA Comment Code: 3170

Comment: You also request comment on how the Agency should account for variation of perchlorate levels over time in public water systems. This is simple: the Agency should act with extreme precaution.

Response: See response to comment code 6120.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28810
EPA Comment Code: 3170

Comment: c. On how the Agency should account for the variation of perchlorate levels over time, based on estimating the number of systems, entry points and sampling.

NRDC Response: If EPA plans to consider the low-end estimate of the population exposed, it must develop a justifiable estimate.

As part of the occurrence analysis, EPA attempted a high-end and a low-end estimate of the population exposed to perchlorate from contaminated drinking water. The high-end estimate, which is the population served by a system with a contaminated entry-point is an appropriate point to use. However, EPA did not employ the best method to estimate population exposure for the low-end estimate. For systems with multiple entry points, EPA estimated an equal proportion of the population was served by each entry point. However, EPA acknowledged that "[t] his approach may provide either an overestimate or an underestimate of the population served by the affected entry point" but failed to provide any reasonable uncertainty analysis. An uncertainty analysis is a mathematical measure of the "goodness" of the result, and therefore our confidence in it. With such an analysis it is impossible to determine the fitness of the value as a basis for making regulatory decisions related to health protection or scientific quality. Therefore, EPA cannot justify using this estimate to model the occurrence of and exposure to perchlorate in drinking water.

There are two problems with assuming that every entry point equally serves a population. First, it is possible that one entry point could serve a large majority of the population and other entry points serve many fewer. Basing the estimate on the proportion of the flow rate of water sent to the system by a given entry point would provide a more accurate representation of the population exposed. Second, having a detection at one entry point does not preclude the possibility that other entry points in the system are also contaminated. For example, one groundwater source may distribute

water to multiple wells which separately contribute water to a system. Therefore, assuming that one contaminated entry point contributes equally to the flow of the entire distribution system is a weak way to estimate the population exposed. Because EPA can neither determine whether this estimation is an overestimate or an underestimate, or provide an analysis of the uncertainty, it should not be used as part of the regulatory determination for perchlorate.

NRDC Response: Estimating the water systems with at least one entry point with a sample above the detection limit is appropriate for the perchlorate regulatory determination.

The perchlorate monitoring program was not designed to specifically detect high levels of perchlorate. While we are not aware of evidence that there are large fluctuations of perchlorate levels in groundwater, detecting perchlorate in drinking water is a signal of a bigger, not smaller, contamination problem. When sporadic sampling is conducted in a system - such as taking a single quarterly or semi-annual sample - detections of contamination are a reflection of a widespread problem. It much more likely that a monitoring program would miss detections and particularly elevated spikes, rather than catch them. Much like searching for a needle in a haystack,if you find one, it is likely because there are many more; however if you don't find one, that does not mean there are none. Therefore, each finding of contamination in monitoring data should be treated seriously, as if it is representative of a widespread problem.

Response: For a discussion on variation of perchlorate levels over time see response to comment code 3170. For a discussion of the analysis EPA used to derive the population estimates that EPA considered in the final regulatory determination see response to comment ID 28525 under comment code 3140. EPA believes that an uncertainty analysis is unnecessary due to the fact that the Agency not only considered central value estimates, as the commenter requested, but the Agency evaluated high end estimates as well. Please see response to comment ID 20952 under comment code 3140.which explains in detail what EPA did to account for high and low end population estimates. EPA agrees that each finding of contamination should be taken seriously and that is part of the reason that we have determined that perchlorate occurs or there is a substantial likelihood that perchlorate will occur with a frequency and at levels of public health concern in public water systems.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28894
EPA Comment Code: 3170

Comment: 3. EPA requests comment on how the Agency should account for the variation of perchlorate levels over time in public water systems. EPA believes that estimating the number of systems, entry points and populations with at least one detection above the HRL is appropriate for the perchlorate regulatory determination because a single quarterly or semiannual sample more closely reflects the short term exposure during life stages of concern (i.e., fetuses, preterm newborns, infants and young children). However, EPA requests comment on whether the Agency should consider other approaches such as estimating the number of systems, entry points and populations with two or more detections above HRL or some other approach.

As discussed above, there are fundamental scientific and statistical issues with the UCMR1 database for estimating current exposures to perchlorate in drinking water, so any application of the data therein would be unreliable. First, UCMR1 data are likely to overestimate current exposure concentrations because data were collected from 2001-2005 and subsequent remediation and treatment has reduced these concentrations, and approximately half of the perchlorate water samples in the UCMR1 database are from untreated source waters. Second, data in the UCMR1 database are insufficient for estimating population sizes because, for PWSs with multiple entry points to the distribution system, the database does not specify the size of subpopulations distributed water from specific entry points where perchlorate was detected.

Response: EPA acknowledges that there may be sources that had detected perchlorate from UCMR1 monitoring that are either no longer being used or are being treated per the requirements of maximum contaminant levels established in California and Massachusetts; however, the 1996 amendments to the Safe Drinking Water Act require the Agency to consider the best available, peer reviewed science when developing drinking water standards. In applying these principles, "best available" usually refers to the availability at the time an assessment is made. UCMR data is the most extensive nationally representative occurrence data for perchlorate in public water systems; therefore, EPA analyzed this data and additional occurrence data in making a regulatory determination for perchlorate as required by SDWA Section 1445.

EPA disagrees that data in the UCMR1 database are insufficient for estimating population sizes. EPA presents in today's Federal Register notice a range of estimates of the population served by PWSs that had at least one sample with perchlorate concentrations greater than the threshold concentrations. The population range represents both a high end estimate, as well as a central value estimate, both derived using the UCMR 1 monitoring data. The high end estimate of the population served drinking water above a threshold is derived by adding the entire system population of all PWSs in which at least one sample was found to contain perchlorate above the threshold. Many PWSs have multiple entry points into which treated water is pumped for distribution to their consumers. For the PWSs with multiple entry points, it is unlikely that the entire service population receives water from the one entry point with the highest single concentration. Therefore, EPA also provides a central value estimate of the population served water with perchlorate above a threshold in today's notice. EPA developed this central value estimate by assuming the population was equally distributed among all entry points and added only the proportion of the total population served by those entry points in a PWS that had at least one sample with perchlorate concentrations greater than the threshold.
In regards to the commenter's concern that approximately half of the perchlorate water samples in the UCMR1 database are from untreated source waters, please see response to comment ID 28893 under comment code 3160.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Department of Environmental Protection (NJDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0527
EPA Comment ID: 28915
EPA Comment Code: 3170

Comment: As discussed in the notice, short-term exposures during sensitive life stages are of concern for perchlorate. We agree that the short time frame of concern should be considered in evaluating perchlorate's occurrence. The NJDEP (2009) MCL proposal considers the short

timeframe of concern for perchlorate in its notification and monitoring requirements. If a public water system receives results of a sample which exceed the MCL, a confirmation sample must be taken within 72 hours, as opposed to within two weeks for contaminants with chronic health effects. Enforcement of the MCL will be based on the average of the initial sample and the confirmation sample. Also, public notification of an MCL violation must take place with 14 days, as opposed to 30 days for contaminants ith chronic health effects.

Because of the short time period of exposure that is of concern for perchlorate, we agree with USEPA that data for systems, entry points, and populations with at least one detection above the HRL should be used in the regulatory determination. We agree that it is appropriate to base the occurrence analysis for the regulatory determination on the maximum concentration detected rather than on the average concentration.

Response: See response to comment code 3170. EPA agrees with the commenter in regards to basing the occurrence analysis on the maximum concentration detected.

EPA Comment Code: 3200 Supplemental drinking water occurrence data from California and Massachusetts

Individual Comments
Commenter Name: Pete McHugh
Commenter Organization: Santa Clara County Board of Supervisors
EPA Document ID: EPA-HQ-OW-2008-0692-0681
EPA Comment ID: 20021
EPA Comment Code: 3200

Comment: Perchlorate is a contaminant found in drinking water in California and at least 34 other states. It interrupts the uptake of iodine in the thyroid and may adversely affect thyroid function, which can then interrupt many hormones in the body. Infants, children, and pregnant women are particularly vulnerable populations.

As of 2005, there were 456 drinking water sources with perchlorate detections in 12 counties in California. In our county, an 18 square mile plume of perchlorate contamination requires the monitoring and remediation of hundreds of water wells. Although the source of Santa Clara County's perchlorate contamination and discharger has been identified, drinking water quality is not expected to return to baseline levels for at least 12 years at best.

Response: Using the criteria mandated by the 1996 SDWA Amendments, EPA has determined that regulation of perchlorate in drinking water systems presents a meaningful opportunity to reduce health risk for persons served by public water systems. See response to comment code 6120.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28829
EPA Comment Code: 3200

Comment: Population Estimates

AMWA agrees with EPA that its population estimate is high for systems with at least one perchlorate detection and multiple entry points into the distribution system. This is because EPA based the estimate upon the assumption that an entire system's population would be served water from the entry point with the perchlorate detection. However, in systems with multiple entry points, AMWA agrees it is unlikely that the system's entire service population would receive water that contains perchlorate at the highest concentration detected at a single entry point.

In addition, AMWA agrees with comments referenced by EPA on page 41890 of the FR notice that some states have higher concentrations of perchlorate in drinking water than others. In addition, the exposure to perchlorate of the population in states that already have regulatory limits for perchlorate will be capped at those levels. For example, staff from the Massachusetts Department of Environmental Protection indicated to AMWA that it will possibly require the PWS with the highest concentration of perchlorate during the commonwealth's last compliance sampling round to shut

down its well and find a new source of water for its service population. Compliance data for the Los Angeles Department of Water and Power (Appendix A [see PDF docket ID EPA-HQ-OW-2009-0494]) shows very few detections, with all samples below California's MCL of 6 ppb.

With regard to UCMR data, many of the utilities in the southwest and western states with perchlorate detections have since seen their concentrations drop. Whether because of state standards, local cleanups at the Tronox (formerly Kerr McGee) facility or for other reasons, EPA must take this into consideration in its final population estimates. For example, SNWA had perchlorate detections in 2003 ranging from 10 - 17 ppb. Today the concentrations range from 1 to 3 ppb. There are many utilities in CA and AZ that are served by Metropolitan Water District (MWD) of Southern California and the Central Arizona Project that had detections in the range of 3 to 6 ppb in 2002 to 2004 that have not had detections of perchlorate in the last 2 years. For example, please see the data from Consumer Confidence Reports from Phoenix (http://phoenix.gov/ftpalias/payf/qualre05.pdf) and Scottsdale (http://www.scottsdaleaz.gov/AssetFactory.aspx?did=28404). In addition, AMWA is also providing annual average perchlorate concentrations from the Alfred Merritt Smith Water Treatment Facility (AMSWTF) at the Southern Nevada Water Authority (Appendix B [see PDF docket ID EPA-HQ-OW-2009-0297-0494]), and MWD data from the Whittsett intake (Appendix C [see PDF docket ID EPA-HQ-OW-2009-0297-0494]). This is raw water data from the Colorado River intakes at these utilities, which is blended with local water supplies.

EPA also should take care to recognize in its population exposure estimates the differences between perchlorate in ground water and surface water. Many groundwater systems do not run all of the system's wells continuously. Wells with higher concentrations of perchlorate may be blended with lower concentrations, causing a diluting effect. Concentration of surface water sources may change due to precipitation. These factors could cause EPA's estimates to be more conservative than stated in the NODA.

It is important for EPA to properly characterize its estimates of the potential population exposed to perchlorate. AMWA recognizes that these estimates include ranges, but the best data available must be used so that these estimates are as thoughtful and accurate as possible. Overestimating the populations affected would effectively lead to an overestimation of the benefits. Overestimating populations affected by perchlorate exposure in drinking water could also effectively build a basis for a body of literature that mischaracterizes the situation, which could then be perpetuated and misused as the information is referenced in the future.

Response: EPA acknowledges that there may be sources that had detected perchlorate from UCMR1 monitoring that are either no longer being used or are being treated per the requirements of maximum contaminant levels established in California and Massachusetts; however, the 1996 amendments to the Safe Drinking Water Act require the Agency to consider the best available, peer reviewed science when developing drinking water standards. In applying these principles, "best available" usually refers to the availability at the time an assessment is made. UCMR data is the most extensive nationally representative occurrence data for perchlorate in public water systems; therefore, EPA analyzed this data and additional occurrence data in making a regulatory determination for perchlorate.
EPA agrees that it is important to properly characterize the estimates of potential population exposed to perchlorate. Please see response to comment ID 28810 in comment code 3170.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28838
EPA Comment Code: 3200

Comment: With regard to using data from the Commonwealth of Massachusetts to help characterize the distribution of very low perchlorate concentration occurrence, AMWA is concerned about extrapolating these data to determine a nationwide distribution for two reasons. First, 89% of public water systems in Massachusetts are solely groundwater systems. In addition, a large number of these systems are non-community water systems. Secondly, the mechanics of perchlorate persistence and occurrence in ground water across the country differ due to factors such as soil retention, subsurface geology, etc.

Therefore, AMWA recommends that EPA extrapolate this data nationwide only for systems that use groundwater, taking care to recognize the proportion of Massachusetts data that are community water systems vs. non-community water systems as well as the differences in other factors that would likely affect these numbers.

Response: EPA did not extrapolate data from Massachusetts nationwide to aid in the determination of a regulation for perchlorate. EPA did analyze the best available and most extensive nationally representative occurrence data from UCMR along with additional occurrence data, and concluded that regulation of perchlorate was warranted. The Agency evaluated supplemental drinking water monitoring data for perchlorate from California and Massachusetts, and believes that these States' monitoring results are generally consistent with the results EPA collected under the UCMR 1.

EPA Comment Code: 3300 Other drinking water occurrence studies, models, and data for EPA to consider (besides UCMR 1 and California and Massachusetts data already evaluated)

Response to Code 3300: Thank you for providing additional data on the occurrence of perchlorate. In August 2009, the Agency sought comments on additional approaches to analyzing data related to EPA's perchlorate regulatory determination. These additional comments were sought in an effort to ensure consideration of all the potential options for evaluating whether there is a meaningful opportunity for health risk reduction of perchlorate through a national primary drinking water rule. EPA evaluated the additional occurrence data received and has considered it along with the UCMR 1 data, which is currently the best available and most extensive nationally representative monitoring program for perchlorate in public water systems.

Using the criteria mandated by the 1996 SDWA Amendments, EPA has determined that regulation of perchlorate in drinking water systems presents a meaningful opportunity to reduce health risk for persons served by public water systems. See response to comment code 6120.

Individual Comments
Commenter Name: Douglas, J. Feldman, PE
Commenter Organization: Office of Water Resources, Suffolk County Department of Health Services (SCDHS)
EPA Document ID: EPA-HQ-OW-2008-0692-0297
EPA Comment ID: 19753
EPA Comment Code: 3300

Comment: The Suffolk County Department of Health Services (SCDHS), located within the County of Suffolk, in New York State, has conducted a search of our records for the past 10 years as it relates to sampling for the chemical perchlorate. The Department has found that of the 5882 samples obtained for perchlorate analyses, between 1998 and 2008, approximately 420 samples were found to contain perchlorate with concentrations that ranged between 1ppb and 49 ppb - with the mean value of 7.17 ppb. This data indicates that approximately 7% of these samples that were checked for perchlorate contained the chemical. It should be noted that of the 420 samples that were positive, 18 were found in community water supply distribution systems; 49 were found in non-community public water supply wells, and 351 were obtained from private wells.

The Long Island aquifer has been designated as "sole source" by the USEPA and is particularly sensitive to perchlorate discharges, due in part to the sand and gravel material that exist above and within our aquifer systems. The Department has been involved with determining and remediating the sources of perchlorate plumes impacting public and private wells within our County. An extensive amount of time, effort and cost was expended by the Department in performing these tasks.

Response: Please see the response to comment code 3300.

Commenter Name: Marcia Willhite
Commenter Organization: Illinois Environmental Protection Agency

EPA Document ID: EPA-HQ-OW-2007-0068-0155
EPA Comment ID: 20258
EPA Comment Code: 3300

Comment: The Illinois EPA has detected and confirmed the presence of these contaminants in soil and potable resource groundwater. Perchlorate has been found at: Crab Orchard National Wildlife Refuge (1,200 micrograms per liter ("µg/l")), Savanna Army Depot (1.2 to 12 µg/l), and Chanute Air Force Base (2.9 µg/l). In addition, there are several other potential sites where it is suspected that perchlorate will be found, but the groundwater has not been tested for perchlorate.

Response: Please see the response to comment code 3300.

Commenter Name: Kathy M. Kinsey
Commenter Organization: Maryland Department of the Environment
EPA Document ID: EPA-HQ-OW-2008-0692-1421
EPA Comment ID: 20427
EPA Comment Code: 3300

Comment: A Uniform Federal Drinking Water Standard is Necessary to Protect Public Health

On the merits of EPA's preliminary determination, based on an initial review, the Department submits that perchlorate is present in ground and surface drinking water at levels of public concern and that establishment of a drinking water standard presents a meaningful opportunity to reduce the health risk perchlorate presents, particularly to the vulnerable and sensitive subpopulations - pregnant and lactating women, fetuses, and young children. There are no technological impediments to removing perchlorate from ground or surface water. Technology capable of removing perchlorate from ground and surface water is already in use. For larger surface water systems eliminating or reducing the source of the contamination would likely be the most practical solution.

Section 1412(b)(1)(A) of the Safe Drinking Water Act requires EPA to establish a maximum contaminant level for a contaminant if: (1) the contaminant may have an adverse effect on the health of persons; (2) the contaminant occurs or presents a substantial likelihood that it will occur in public water systems at a frequency and at levels of public concern; and (3) EPA determines that regulation of the contaminant presents a meaningful opportunity for health risk reduction for persons served by public drinking water supplies. In the case of perchlorate, each of the criteria is satisfied.

There is no genuine dispute that perchlorate may have an adverse effect on human health. Perchlorate is known to interfere with thyroid function. Lower thyroid hormone levels can cause changes that adversely impact brain development. In its preliminary determination, EPA acknowledges that at sufficiently high doses, perchlorate can interfere with thyroid function in pregnant women, fetuses, newborns and young children.

In Maryland, perchlorate is present at significant levels in ground and surface water at three Department of Defense facilities. At Aberdeen Proving Ground in Harford County, Maryland, perchlorate has been detected in groundwater at seven different locations and at levels as high as 350 parts per billion ("ppb"). Perchlorate from other areas of the installation has contaminated the water supply for the City of Aberdeen. In the absence of a federal drinking water standard, the State has set an advisory level of 1 ppb for the City treatment system's finished water.

Although no public drinking water supply wells have been impacted, perchlorate levels in ground water at the Naval Support Facility at Indian Head have been detected at levels as high as 2,900 ppb. At a number of other sites in Cecil County, Maryland, perchlorate contamination was detected in ground water monitoring wells at levels as high as 230,000 ppb in the late 1990's. In the one case where perchlorate contamination has impacted the drinking water supply, the Department has provided bottled water to affected residents and required installation of a treatment system to address the contamination. Perchlorate contamination has also been detected in the Potomac River, the source of drinking water for millions of Maryland, Virginia, West Virginia and District of Columbia residents. EPA sampling detected perchlorate levels up to 8 ppb in one of Maryland's Potomac River water supply intakes.

Establishing a federal drinking water standard that would protect the millions of people, including pregnant women, infants and young children, who are served by drinking water that is currently contaminated or at risk of contamination by perchlorate is necessary to protect public health.

Response: EPA agrees with the commenter that the three criteria for determining whether a contaminant should be regulated from SDWA section 1412(b)(1) are satisfied for perchlorate. Please see the responses to comment codes 6120 and 3300.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association
EPA Document ID: EPA-HQ-OW-2008-0692-1424
EPA Comment ID: 20438
EPA Comment Code: 3300

Comment: Occurrence

As noted above, one of the criteria for evaluating the need for potential regulatory actionis occurrence. In 2005, AWWA prepared an assessment of data collected under the first Unregulated Contaminant Monitoring Rule (UCMR1). AWWA recently completed a follow-up of this initial assessment using the final UCMR1 data set considered by EPA in this proposed decision. There were very subtle differences, in total numbers, but that did not result in a significant difference in the overall findings. This analysis is summarized below and has been submitted to a peer-reviewed journal and is pending publication.

The evaluation by Brandhuber et.al. (pending publication) consolidated existing potable water perchlorate occurrence information taken from UCMR1 and other recently completed occurrence studies. The detection of perchlorate in drinking water was determined to be geographically widespread but at very low concentrations. Significantly, there was little correlation between perchlorate detection in drinking water and known points of perchlorate release to the environment identified by the USEPA. Perchlorate has been detected in drinking water in at least 26 States and Puerto Rico and in approximately 5% of the nation's large community water systems (>10,000 population served). When detected, perchlorate was typically present at concentrations of less than 12 ug/L and was generally found in less than one half of the sources for systems which sampled multiple sources. No statistically significant difference in the rate of perchlorate occurrence between surface and ground waters was identified.

Extrapolating the results of the occurrence studies reviewed by this report, it appears that nationally less than 1% of all drinking water systems would be impacted if an MCL of 20ug/L were established. An MCL of 2 ug/L could impact approximately 4% of public water systems nationally. At this level, regional impacts in California and Texas would be greater due to the higher geographical concentration of detections in those states. Yet it should be noted that water systems in Massachusetts, New Jersey and California have already established regulatory limits of 2 ug/L, 5 ug/L and 6 ug/L respectively, thereby capping the population exposure potential from community drinking water sources in those states.

The estimated population exposure calculated from UCMR1 findings has also been greatly reduced by the effectiveness of mitigating contamination sources on the Colorado River to levels below 2 ug/L. This reduction in levels in the Colorado River alone represents a reduction in the exposure potential of approximately 20 million persons in several western states, primarily California and Arizona. In addition, a recent telephone survey of water systems detecting perchlorate indicated that at least 50 MGD of water production has been taken off line nationally due to the presence of perchlorate since UCMR1 monitoring was completed.

Response: Thank you for providing the additional analysis of data on the occurrence of perchlorate. EPA notes that New Jersey proposed an MCL of 5 µg/L in April 2009, but this standard has not been finalized. In July 2006, Massachusetts set an Maximum Contaminant Level (MCL) of 2 µg/L. Additionally, In October 2007, California set an MCL of 6 µg/L. Please see response to comment ID 28755 in comment code 3300. Using the criteria mandated by the 1996 SDWA Amendments, EPA has determined that regulation of perchlorate in drinking water systems presents a meaningful opportunity to reduce health risk for persons served by public water systems. See response to comment code 6120.

Commenter Name: Paul J., P.E. Ponturo
Commenter Organization: Long Island Water Conference
EPA Document ID: EPA-HQ-OW-2008-0692-1260
EPA Comment ID: 20622
EPA Comment Code: 3300

Comment: November 7, 2008

Water Docket Environmental Protection Agency Mailcode 2822 T 1200 Pennsylvania Ave., NW Washington, DC 20460

Re: Docket ID No. EPA-HQ-OW-2008-0692 Drinking Water: Preliminary Regulatory Determination on Perchlorate, FR 10/10/08

Gentlemen:

On behalf of the Long Island Water Conference, an association of public water supply professionals in Nassau and Suffolk Counties in NY, I am pleased to present our comments on the referenced preliminary regulatory determination.

Our member suppliers have a long history of responsiveness in meeting the increasing needs for comprehensive water supply monitoring, research and groundwater protection programs. We have

worked cooperatively with our regional regulatory agencies to provide monitoring and oversight that dramatically exceeds federal EPA requirements. Aggressive monitoring is necessary and desirable in protecting public health. We have also worked with regional regulatory agencies in water supply and water resource management studies and supported the integration of local regulations which combine discharge controls, land use, and the storage of hazardous substances into an advanced source water protection system.

Long Island was one of the first designated Sole Source Aquifer systems in the United States, and with a total population of nearly three million, is considered to be one of the most intensively used and critical Aquifer systems in the country.

This preliminary regulatory determination therefore is significant to every public water supplier on Long Island. Approximately 250 community water supply wells in Nassau and Suffolk County have indicated detection of perchlorate in concentrations greater than 1 ppb. Consistent with EPA's occurrence evaluation, a much smaller number of sources exhibit concentrations greater than 5 ppb (approximately 25) or 10 ppb (approximately 10). The Health Reference Level (HRL) of 15 ppb used by EPA to reach this determination is close to the NYS Department of Health's Action Level (discussed below); no Long Island public water supplier customer is being currently exposed to concentrations in excess of this Level.

Response: Please see the response to comment code 3300.

Commenter Name: Paul J., P.E. Ponturo
Commenter Organization: Long Island Water Conference
EPA Document ID: EPA-HQ-OW-2008-0692-1260
EPA Comment ID: 20623
EPA Comment Code: 3300

Comment: We do not have a technical basis upon which to criticize EPA's determination. Based upon its interpretation of Safe Drinking Water Act criteria, EPA has determined there is not a "meaningful opportunity for health risk reduction" through a national drinking water regulation. EPA's conclusion is based upon its own analysis of available data indicating that perchlorate was found at levels of public health concern (the HRL) in less than 1 percent of public drinking water systems sampled.

However we do wish to point out that without a greater understanding of perchlorate formation processes and the possibility that unmeasured perchlorate may exist in other salts in common use, one may still lack statistical confidence in utilization of the UCMR data to estimate population exposures in drinking water. Unlike other parts of the country, a clear source for many of Long Island's perchlorate contamination occurrences has not emerged over the past 10 years. The highest recorded perchlorate concentration in a well on Long Island was traced to a completely unregulated activity, as described below.

Perchlorate monitoring of public water supplies on Long Island began in the spring of 1998. Initially in response to perchlorate detection reports elsewhere in the US, the Suffolk County Water Authority (SCWA) voluntarily collected samples from wells at five wellfields. The samples were sent to the Montgomery Watson Laboratory for analysis. Of the initial sample results one well - #3 at the Old Country Road wellfield in Westhampton - indicated a concentration of perchlorate of 30 ppb.

The SCWA removed this well from service. At the end of 1998, NY State Department of Health provided an Action Level of 18 ppb. This well later showed concentrations as high as 127 ppb in samples collected during subsequent test pumping. Initial thoughts were directed to the former military uses of property immediately upgradient of the well at a former BOMARC missile site. This was discounted, upon submission of evidence that solid fuel rockets were not deployed at this site.

By late 1998, attention turned to a review of more recent activities subsequent to the takeover of the BOMARC site by Suffolk County - specifically the Suffolk County Police Department (SCPD) practice of disposal of confiscated fireworks and munitions by burning. Between November 1998 and February 2000, a total of 18 profile wells were installed by the Suffolk County Department of Health Services' (SCDHS) Bureau of Groundwater Resources in locations upgradient and downgradient of the fireworks disposal pit, which was located in the northwest corner of the site. Groundwater flow direction and water quality data appeared to eliminate other activities in the area as potential sources. Perchlorate was detected in 9 test wells downgradient of the pit, in concentrations as high as 3,370 ppb. Although the pit and burning practices have been modified, fireworks disposal at the site continues, and to date such disposal is not covered under any NY State environmental regulation. In subsequent years, SCDHS also investigated the contamination of a number of private wells and one non- communitysupply well in Yaphank, NY, which later traced to fireworks testing and a practice of stabilizing "dud" fireworks by a process called "soaking." This process utilizes water indrums to leach out the perchlorate from the dud, stabilizing the firework for subsequent disposal by burning.

Local laboratory capacity has been developed at SCWA, SCDHS and at private labs to assist in the monitoring effort, which began in earnest before the UCMR implementation date, and monitoring continues.

Response: Please see response to comment code 3300.

Commenter Name: Mic Stewart
Commenter Organization: Metropolitan Water District of Southern California
EPA Document ID: EPA-HQ-OW-2008-0692-1784
EPA Comment ID: 20661
EPA Comment Code: 3300

Comment: November 6, 2008

Attention: Docket ID Number EPA-HQ-OW-2008-0692 OSWER Docket EPA Docket Center Mailcode: 2822T Environmental Protection Agency 1200 Pennsylvania Ave., NW Washington, DC 20460

Dear Environmental Protection Agency:

The Metropolitan Water District of Southern California (Metropolitan) is submitting comments on U.S. Environmental Protection Agency's (EPA's) Preliminary Regulatory Determination on Perchlorate (73 Federal Register 60262). The proposed action by the EPA not to regulate the drinking water contaminant perchlorate will affect how state and local officials can respond to localized perchlorate contamination.

Metropolitan is a regional water supply agency that provides supplemental water to nearly 19 million people throughout the southern California area. Our major source of supply, the Colorado River, was contaminated from industrial production of perchlorate for solid rocket fuel and subsequent improper disposal methods. Perchlorate contaminated groundwater seeping into Lake Mead through the Las Vegas Wash area found its way into the Colorado River, which supplies Metropolitan and other downstream users. Levels as high as 20 parts per billion (ppb) were detected in Lake Mead and levels as high as 9 ppb have been detected at the intake to Metropolitan's conveyance system. Following the detection of perchlorate in the Colorado River, Metropolitan along with the EPA and regulatory agencies in Nevada, organized the forces necessary to successfully treat and decrease the sources of perchlorate loading. Since 2006, monitoring has indicated levels at or below 2 ppb entering Metropolitan's conveyance system.

Response: Please see the response to comment code 3300.

Commenter Name: Stephen A. Owens
Commenter Organization: Arizona Department of Environmental Quality
EPA Document ID: EPA-HQ-OW-2008-0692-1785
EPA Comment ID: 20665
EPA Comment Code: 3300

Comment: November 7, 2008

Comment Clerk Water Docket Environmental Protection Agency Mail Code: 2822T 1200 Pennsylvania Ave., NW. Washington, DC 20460

Re: Arizona Department of Environmental Quality Comments on Federal Preliminary Regulatory Determination on Perchlorate Docket EPA-HQ-OW-2008-0692

Dear Sir:

In response to the notice in the Federal Register of October 10, 2008 (Volume 73, Number 198) the Arizona Department of Environmental Quality (ADEQ) is offering comments on the Preliminary Regulatory Determination on Perchlorate. ADEQ offers these comments in role of the delegated authority responsible for protecting public health in Arizona through rules promulgated under the Federal Safe Drinking Water Act.

Perchlorate contamination is known to be present in Arizona water supplies. Arizona, along with other arid western states, relies heavily upon the Colorado River as a critical source of our population's drinking water supply. The overall "health" and water quality of the Colorado River and other surface water sources are of the utmost concern for Arizona. Perchlorate contamination has impacted the Colorado River due to industrial sources in the Las Vegas area. The source of this contamination has been controlled more effectively by the responsible parties; however the risk of perchlorate contamination in the Colorado River water supply still exists.

A Consumer Confidence Report issued by the City of Phoenix (City) in 2007 is one example of a direct perchlorate related impact on Arizona citizens. According to City records, roughly ninetyeight percent of all potable water produce annually is derived from surface sources, including water from the Colorado River. In 2004, the City collected 392 finished water distribution samples (as a

precautionary measure) to gather more information on the occurrence of perchlorate in the public water system supply. Thirty-nine of those samples tested at, or above, the minimum detection level of four (4) part per billion for the presence of perchlorate.

Perchlorate contamination is not strictly limited to surface waters of the Southwest. A perchlorate occurrence study conducted by ADEQ (Perchlorate in Arizona: Occurrence Study of 2004) revealed numerous groundwater sources with detectable levels of perchlorate. One well located in Yuma County tested positive in 2004 for levels of perchlorate in the 15 parts per billion (ppb) range. Groundwater is a critical source of drinking water in Arizona and under Arizona law all aquifers in the state are designated by statute for drinking water use.

Response: Please see the response to comment code 3300.

Commenter Name: Ron Curry
Commenter Organization: New Mexico Environment Department
EPA Document ID: EPA-HQ-OW-2008-0692-1796
EPA Comment ID: 20933
EPA Comment Code: 3300

Comment: Nevertheless, the limited available drinking water data that the Environment Department has reviewed show significant perchlorate contamination in several public drinking water systems around the State. In the Department's view, perchlorate contamination in drinking water occurs at levels and at a frequency that is a public health concern in New Mexico.[FN2: See SDWA [section] 1412(b) (1)(A)(ii), 42 U.S.C. [section] 300g-1(b)(1)(A)(ii) (Westlaw 2008).]

At Cannon Air Force Base, near Clovis, New Mexico, the Environment Department received data in 1999 showing perchlorate concentrations of 46 micrograms per liter (ug/L) in production well PW-2 and 21 ug/L in production well PW-7. These wells are both active drinking water production wells that serve users on the Base.[FN3: N.M. Environment. Dep't, Perchlorate Survey 2001 Final Report, vol. 1, tab "Cannon" (unpublished compilation).] Data that the Environment Department gathered in 2001 from Cannon showed perchlorate contamination of 23.5 ug/L in PW-12, another drinking water production well.[FN4: Id.] Data collected from the system in 2003 and submitted to the Environment Department under the Unregulated Contaminant Monitoring Ruleshows a perchlorate level at 30 ug/L.[FN5: Safe Drinking Water Information System, State version (SDWIS/State). The State has not verified the accuracy of this data.] In addition, the Government Accountability Office (GAO) has compiled data on perchlorate contamination throughout the United States, including New Mexico. In its 2005 report, GAO similarly reported perchlorate at 46 ug/L in drinking water at Cannon Air Force Base.[FN6: GOVERNMENT ACCOUNTABILITY OFFICE, A SYSTEM TO TRACK SAMPLING AND CLEANUP RESULTS IS NEEDED, AT 37 (GAO-05-462) (May 2005).]

At the Melrose Bombing Range, also near Clovis, the Environment Department received data in 1999 showing perchlorate contamination in production well PW-11, an active drinking water production well for the facility, at 25 ug/L.[FN7: N.M. Environment. Dep't, Perchlorate Survey 2001 Final Report, vol. 2, tab "Melrose" (unpublished compilation).] Data the Environment Department obtained in 2001 from Melrose showed perchlorate concentrations of 30.3 ug/L and 40.7 ug/L in PW-11(shown as MAFR Well-11), and a perchlorate concentration of 5.52 ug/L in PW-13 (shown as MAFR Well-13), an other on-site facility drinking water supply wel1.[FN8: Id.]

At Kirtland Air Force Base, data collected in 2004 show perchlorate contamination in Well #17, a drinking water supply well, at 12.6 ug/L.[FN9: Letter from Carl J. Lanz, Chief, Restoration Section, Kirtland Air Force Base, to Sandra Martin, Chief, Hazardous Waste Bureau, N.M. Environment Dep't (Mar. 31, 2004).] Kirtland is located adjacent to the City of Albuquerque, which is the State's largest metropolitan area having a population over 500,000. Yet there is very little available data on perchlorate in drinking water on and around Kirtland.

The GAO also reported perchlorate contamination in the municipal drinking water supply for the City of Deming, New Mexico at 20 ug/L, and for the City of Des Moines, New Mexico at 5 ug/L. GAO reported perchlorate in the drinking water supply for the City of Clovis, New Mexico, operated by the American Water Company, at 7 ug/L. GAO also reported perchlorate in the water supply for the community of Mountain View Albuquerque, in the South Valley of Albuquerque, New Mexico, at 5 ug/L.

The Environment Department has gathered additional data demonstrating widespread perchlorate contamination in groundwater at several military installations and nuclear weapons facilities throughout the State. In many cases, this contamination threatens present and future drinking water supplies.

At Los Alamos National Laboratory, perchlorate contamination has been monitored in groundwater beneath much of the 40-square mile facility. Of particular significance, sampling conducted beginning in 2005 shows perchlorate concentrations ranging between 30 ug/L and 256 ug/L in intermediate wells located in Mortandad Canyon. More recent data shows that this contamination has remained relatively constant. A deeper monitoring well, Well R-15, shows a perchlorate concentration of 7 ug/L. The highest contamination, 256 ug/L in intermediate well MCOBT-4.4, is within 2000 feet from PM-5, a municipal drinking water production well for Los Alamos County. Low concentrations of perchlorate, below 1 ug/L, have been detected in PM-5. Neither the sources of the perchlorate contamination, nor the nature and extent of the perchlorate plume, are fully characterized. The perchlorate contamination threatens the Los Alamos County water supply, which serves approximately 20,000 people.

At Sandia National Laboratories, adjacent to the City of Albuquerque, perchlorate has been found in the EOD Hill monitoring well at concentrations ranging from 680 ug/L to 4300 ug/L. Data from 2006 and 2007 show that perchlorate has been detected in CYN-MW6 monitoring well at concentrations between 6.56 ug/L and 8.93 ug/L. Perchlorate data at Sandia is limited, however.

At the United States Army White Sands Missile Range, near Socorro, New Mexico, high levels of perchlorate contamination in soil and groundwater is widespread. In 2000, perchlorate was detected in 22 of 23 groundwater monitoring wells at concentrations ranging from 5 ug/L to 21,000 ug/L.[FN10: N.M. Environment. Dep't, Perchlorate Survey 2001 Final Report, vol. 2, tab "White Sands" (unpublished compilation).] Currently, the highest concentrations are 19,000 ug/L. The Army has vigorously resisted conducting any corrective action to remedy the contamination.

At Holloman Air Force Base, groundwater data collected in September 1999 showed perchlorate levels of 15.5 ug/L in monitoring well NM-39-02-01, 15.2 ug/L in monitoring well NM-39-02-02, and 38.9 ug/L in monitoring well NM-39-03.

At Kirtland Air Force Base, data collected in 2006 showed perchlorate levels in monitoring well KAFB-2622 at 8.4 ug/L, and in monitoring well KAFB-2624 at 11.0 ug/L. Data collected in 2008 showed perchlorate in the "School House Mesa Well" at 5.19 ug/L. Yet very little groundwater monitoring data has been obtained for perchlorate at Kirtland.

Response: Please see response to comment code 3300.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-2082
EPA Comment ID: 21026
EPA Comment Code: 3300

Comment: 9. Your letter asserts that in the absence of a federal MCL, high perchlorate levels in drinking water will go undetected and therefore national monitoring is needed.

The use of Unregulated Contaminant Monitoring Rule (UCMR) sampling data for regulatory determinations is well established. The nationally- representative UCMR 1 results show that perchlorate does not occur frequently or at levels of public health concern in public water systems. Additionally, as evidenced by more recent sampling results from Lake Mead, the Las Vegas Wash, and the Metropolitan Water District of Southern California (MWD), perchlorate levels continue to decline since the time of the UCMR 1 sampling. The preliminary determination assumes that the concentrations measured in the UCMR 1 survey are still occurring. In fact, levels in many of the highest reported drinking water systems have significantly declined due to source control.

Response: Please see the response to comment ID 28755 in comment code 3300.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21095
EPA Comment Code: 3300

Comment: Additionally, as evidenced by sampling results from Lake Mead, the Las Vegas Wash, and the Metropolitan Water District of Southern California, perchlorate levels continue to decline since the time of the UCMR 1 sampling. The preliminary determination assumes that the concentrations measured in the UCMR 1 survey are still occurring. In fact, levels in many of the highest reported drinking water systems have significantly declined due to source control.

Response: Please see the response to comment ID 28755 in comment code 3300.

Commenter Name: James D. Taft
Commenter Organization: Association of State Drinking Water Administrators
EPA Document ID: EPA-HQ-OW-2009-0297-0525
EPA Comment ID: 28499
EPA Comment Code: 3300

Comment: Comments on interpreting occurrence data - Because many states do not have significant occurrence of perchlorate and some had no occurrence, states are concerned that the burden of a possible rule would fall heavily on these states and their water systems with little actual reduction in health risk for their water consumers. ASDWA is also familiar with new data from Nevada (submitted separately) that indicate a reduction in perchlorate levels since the UCMR data were collected. These data need to be included in the analyses along with the modeling approach and use of census data that are addressed in the specific questions.

Response: EPA acknowledges the commenters concern for a federal perchlorate regulation and that some states had no occurrence during UCMR1 monitoring; EPA analyzed additional occurrence data received along with UCMR data (which is the best available and most extensive nationally representative occurrence database for perchlorate in public water systems known to date) and using the criteria mandated by the 1996 SDWA Amendments, determined that regulation of perchlorate in drinking water systems presents a meaningful opportunity to reduce health risk for persons served by public water systems. See response to comment code 6120. When EPA proposes a NPDWR that includes a maximum contaminant level, EPA will analyze and consider both the costs and benefits that would result from regulation and present these analyses for public comment. See SDWA section 1412(b)(3)(C).

Commenter Name: Mic Stewart
Commenter Organization: Water Quality Section, Metropolitan Water District of Southern California
EPA Document ID: EPA-HQ-OW-2009-0297-0496
EPA Comment ID: 28709
EPA Comment Code: 3300

Comment: September 18, 2009 Attention: Docket ID Number EPA HQ-OW-2009-0297 EPA Docket Center Mailcode: 2822T Environmental Protection Agency 1200 Pennsylvania Ave., NW Washington, DC 20460

Dear Environmental Protection Agency:

The Metropolitan Water District of Southern California (Metropolitan) is submitting comments on U.S. Environmental Protection Agency's (EPA) Drinking Water: Perchlorate Supplemental Request for Comments (74 Federal Register 41883). This EPA notice follows the previously proposed action by the EPA not to regulate the drinking water contaminant perchlorate which will affect how state and local officials can respond to localized perchlorate contamination.

Background on the Southern California Situation

Metropolitan is a regional water supply agency that provides supplemental water to nearly 19 million people throughout the southern California area. Our major source of supply, the Colorado River, suffered significant contamination from industrial production of perchlorate for solid rocket fuel and subsequent improper disposal methods. Perchlorate-contaminated groundwater seeping into Lake Mead through the Las Vegas Wash found its way into the Colorado River, which supplies southern California and other downstream users. Levels as high as 20 parts per billion (ppb) were detected in Lake Mead and levels as high as 9 ppb have been detected at the intake to Metropolitan's conveyance system, located approximately 160 miles south of the Las Vegas Wash.

In 1997, the source of perchlorate contamination in the Colorado River was traced to a chemical manufacturing facility formerly owned by Kerr-McGee Corp., and now owned by Tronox, Inc. Tronox, previously a chemical subsidiary of Kerr- McGee, has assumed the responsibility of the ongoing perchlorate remediation activities in Henderson, Nevada. Another large perchlorate groundwater plume is also present in the Henderson area from a second industrial site, and although not known to have reached Las Vegas Wash yet, remediation activities are ongoing for cleanup of that plume by American Pacific Corporation.

Following the detection of perchlorate in the Colorado River, Metropolitan, along with the EPA and agencies in Nevada including the Nevada Division of Environmental Protection (NDEP), organized the forces necessary to successfully treat and decrease the sources of perchlorate loading. Under NDEP oversight, remediation efforts began in 1998 and the treatment operations became fully operational in 2004. These efforts have reduced perchlorate loading into Las Vegas Wash from over 1,000 lbs/day (prior to treatment) to 60-90 lbs/day since early 2007. These have resulted in over 90 percent reduction of the perchlorate loading entering the Colorado River system.

Perchlorate levels in Colorado River water at Lake Havasu have decreased significantly in recent years from a peak of 9 ppb in May 1998 as a result of aggressive clean-up efforts at Henderson, Nevada (see Figure 1). Levels have remained less than 6 ppb since October 2002, and have been generally less than 2 ppb since June 2006.

Figure 1. Declining Perchlorate Levels at Lake Havasu [see PDF docket ID EPA- HQ-OW-2009-0297-0496]

Response: Please see response to comment code 3300.

Commenter Name: Mic Stewart
Commenter Organization: Water Quality Section, Metropolitan Water District of Southern California
EPA Document ID: EPA-HQ-OW-2009-0297-0496
EPA Comment ID: 28711
EPA Comment Code: 3300

Comment: On January 12, 2009, Tronox filed for Chapter 11 bankruptcy protection (U.S. Bankruptcy Court, Southern District of New York). The company cited the significant environmental liabilities taken on from Kerr-McGee as a primary cause of its financial liabilities. Tronox has indicated plans to restructure the company while continuing its operations. Metropolitan is concerned that the outcome of the bankruptcy proceedings could potentially impede or even reverse the ongoing cleanup efforts aimed at remediating perchlorate contamination entering the Colorado River. If perchlorate treatment in the Las Vegas Wash area were discontinued, modeling results suggest that perchlorate levels in the Colorado River could spike to concentrations as high as 9 ppb in as little as 18 months. This level of perchlorate would result in non-compliance by drinking water utilities with California's existing MCL for perchlorate of 6 ppb.

While the State of California does have a 6 ppb MCL for perchlorate, this drinking water standard is not enforceable outside the State. EPA's role in establishing and enforcing a national drinking water standard for perchlorate will be critical in the long-term remediation of perchlorate contamination in

the Colorado River and hundreds of U.S. Department of Defense sites around the country. Since the detection of perchlorate contamination throughout the southwest region and in hundreds of local groundwater wells, Metropolitan, its member agencies, and the drinking water community have called on the EPA to make a regulatory determination on perchlorate consistent with the tenets of the Safe Drinking Water Act. Metropolitan believes that the unique factors surrounding regional perchlorate contamination in the Colorado River system need to be considered.

Response: The commenters concerns regarding the outcome of the bankruptcy proceedings are outside of the scope of this action. Regarding your comment that EPA "make a regulatory determination on perchlorate consistent with tenents of the Safe Drinking Water Act," using the criteria mandated by the 1996 SDWA Amendments, EPA has determined that regulation of perchlorate in drinking water systems presents a meaningful opportunity to reduce health risk for persons served by public water systems. See response to comment code 6120.

Commenter Name: Mic Stewart
Commenter Organization: Water Quality Section, Metropolitan Water District of Southern California
EPA Document ID: EPA-HQ-OW-2009-0297-0496
EPA Comment ID: 28713
EPA Comment Code: 3300

Comment: Additionally, Metropolitan would like to suggest that EPA take the additional time necessary to review and quantify occurrence data collected by the Agency and by individual states including California to better represent possible exposure and occurrence. Perchlorate occurrence is expected to increase unlike other contaminants on the Contaminant Candidate List such as pesticides that are no longer in use.

Response: Please see the response to comment code 3300.

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 28755
EPA Comment Code: 3300

Comment: The Lower Colorado River System provides drinking water to approximately 26 million residents of Nevada. Arizona, and California through three primary diversions:

1) Southern Nevada Water Authority (SNWA) and Black Mountain Inc. Intakes in Lake Mead, which serve approximately 2 million residents within the Las Vegas Valley (distributed through portions of the City of Las Vegas, the City of Henderson, and Clark County);

2) The Central Arizona Project (CAP) canal, which conveys water from Lake Havasu (near Parker Dam) to several locations throughout Arizona including the Phoenix and Tucson Valleys and serves approximately 5 million residents of Arizona; and

3) The Colorado River Aqueduct operated by the Metropolitan Water District (MWD) of Southern California to convey water from Lake Havasu (near Parker Dam) to several communities in southern

California including several within the greater Los Angeles area and the greater San Diego area. We understand that MWD serves approximately 19 million end users through various wholesale and retail agreements. We also understand that water quality measurements collected and posted by MWD for the Colorado River Aqueduct are tracked under "Whitsett Intake".

Additionally, the Colorado River System also is used for irrigating much of the nation's vegetable crops grown in the Imperial Valley of California and the Yuma, Arizona area. This water is conveyed through the All American Canal from a diversion near Yuma, Arizona to numerous locations in southern California near the US / Mexico International border.

Remediation of perchlorate source areas within the Las Vegas Valley has substantially reduced (by approximately 90 %) the amount of perchlorate entering the Colorado River System (NDEP, 2009c). Corresponding water quality improvements have been realized along the entire southern reach of the Colorado River extending from Lake Mead, though Lake Mohave and Lake Havasu, to the US/Mexico International border. Data collected by numerous entities (i.e., NDEP, SNWA, MWD, CAP, EPA, and others) since approximately 1997/1999 though current have documented the improvements in water quality throughout the lower Colorado River System. The reductions in perchlorate entering the Colorado River System can be observed in the graphs of perchlorate data provided in Appendix A [See PDF docket ID EPA-HQ-OW-2009-0297-0639] and Appendix B [See PDF docket ID EPA- HQ-OW-2009-0297-0640] and are attributable to several successive remediation events including (NDEP, 2009d; NDEP, 2009c):

* initial Seep capture by Kerr McGee (now Tronox) in 1999; * construction of a slurry wall and extraction well field in 2001; * operation a full-scale groundwater treatment system in 2002; * expansion of the Seep area extraction well field in 2003; * transition from an ion exchange system to Fluidized Bed Reactor (FBR) treatment system in 2004; * continued operation and optimization of the FBR and well fields from 2005 through current; * initial installation of an In-situ Bioremediation (ISB) system by AMPAC in 2005; * initial start-up and operation of the ISB system in 2006; and * continued operation and optimization of the ISB system from 2007 through current.

The referenced reduction in perchlorate mass loading to the Colorado River system (via the Las Vegas Wash, a tributary to Lake Mead) were immediately recognized following the initial Seep capture and treatment using disposable ion exchange (IX) resin implemented by Kerr McKee (Tronox) in late 1999. The mass loading values dropped approximately 40% from approximately 900 - 1,000 pounds per day to approximately 500 - 600 pounds per day by December 2001 as can be seen on the "Perchlorate Loading 12-Month Rolling Average" graph in the NDEP maintained Northshore Road data set in Appendix c [See PDF docket ID EPA-HQ- OW-2009-0297-0641] (NDEP, 2009b). Continuous reductions in perchlorate mass are seen in the Northshore Road data beginning with operation of the full-scale remediation system in October 2002. The decrease in perchlorate mass loading continued through conversion to an FBR system in October 2003 and its one-year shake-down period. Decreases in perchlorate mass loading have continued from late 2004 through the present, as Tronox optimized their remediation system and AMPAC initiated remediation of a second perchlorate plume in mid 2006 as can be seen on each of the three data graphs for the Northshore Road dataset in Appendix A [See PDF docket ID EPA-HQ-OW-2009-0297-0639] (NDEP, 2009d). Greater than 90% decrease in mass loading has been sustained since February 2007 (i.e., for more than two and one half years) as can be seen in the Northshore Road tabular data presented in Appendix C [See PDF docket ID EPA-HQ- OW-2009-0297-0641] and the related Breakthrough Curve in Appendix D [See PDF docket ID EPA-HQ-OW-2009-0297-0642]

(NDEP, 2009b; NDEP, 2009a; McGinley & Associates, 2003). These trends are expected to continue.

Water quality improvements within the Colorado River system are documented within the Southern Nevada Water Authority (SNWA) intake data for Lake Mead as can be seen in the Perchlorate Monthly Stream Report provided in Appendix E [See PDF docket ID EPA-HQ-OW-2009-0297-0643] (SNWA, 2009a). Yearly average SNWA Intake data for one of the two existing intakes in Lake Mead show a precipitous drop in perchlorate concentrations from approximately 13.4 ug/L in year 2000, through approximately 10 - 11 ug/L during years 2001, 2002, and 2003, to approximately 2 - 2.5 ug/L in years 2007, 2008, and 2009 as can be seen in the Perchlorate - Yearly Average - AMSWTF Raw Water graph and tabular data provided in Appendix F [See PDF docket ID EPA-HQ-OW-2009-0297-0644] (SNWA, 2009b). These water quality improvements correspond to the significant reduction in perchlorate mass loading to the Colorado River System via the Las Vegas Wash.

Seasonal water quality fluctuations that are present in the Lake Mead data are a result of seasonal lake stratification and mixing events as can be seen in the graph of Saddle Island Intake Data in Appendix E [See PDF docket ID EPA-HQ- OW-2009-0297-0643] (SNWA, 2009a). Lake Mead typically destratifies annually due to changes in temperature and wind driven mixing. The surface waters routinely mix to a depth of 30 - 45 feet below the lake surface level throughout the summer (that allows for stratified water quality conditions) and the surface layer deepens to 100 feet in the autumn. The lake destratifies in the late winter, resulting in more uniform water quality as constituents are dispersed throughout the water column. Therefore, water intake structures (including those at Hoover Dam) will be subject to the water quality present within the water column adjacent to the intake structure and this water quality will change seasonally.

Water quality improvements are also noticeable within the NDEP maintained Willow Beach data set provided in Appendix G [See PDF docket ID EPA-HQ- OW-2009-0297-0645] (NDEP, 2009c). These data were collected from the Arizona side of the Colorado River within Lake Mohave approximately 11 miles downstream of Hoover Dam (Lake Mead). It is thought that these data represent mixed water quality conditions applicable to downstream users. Review of these data shows that perchlorate concentrations have been sustained at less than 4 ug/L, from June 2004 through current as can be seen on the graph of perchlorate concentration and tabular data provided in Appendix G [See PDF docket ID EPA-HQ- OW-2009-0297-0645] (NDEP, 2009c).

Water quality trends at the Metropolitan Water District (MWD) of Southern California Whitsett Intake also show improved water quality over time, with sustained perchlorate concentrations at less than 4 ug/L from June 2004 to November 2005 and less than 2.3 ug/L from November 2005 through present as can be seen in the MWD Whitsett graphical and tabular data provided in Appendix H [See PDF docket ID EPA-HQ-OW-2009-0297-0646] (MWD, 2009). These sustained declines in perchlorate concentrations led to several actions by MWD including:

* Lowering of the reporting (detection) limit from 4 ug/L to 2 ug/ L in September 2003; * Change in analytical methods to EPA Method 331 in January 2007 and EPA Method 332 in July 2008 to permit a 0.1 ug/L reporting limit; and * Change in sample frequency from monthly to quarterly in January 2007. [bullets corrected based on docket ID EPA-HQ-OW-2009-0297-0649]

Similar water quality trends are reported by the Central Arizona Project (CAP) for perchlorate concentrations measured in CAP Intake water near Lake Havasu, Arizona. The similar water quality results reported from MWD and CAP are a result of both entities drawing source water from the same reservoir (Lake Havasu) near Parker Darn, Arizona.

Response: Thank you for providing additional data on the occurrence of perchlorate. EPA acknowledges that there may be sources that had detected perchlorate from UCMR1 monitoring that are either no longer being used or are being treated; however, the 1996 amendments to the Safe Drinking Water Act require the Agency to consider the best available, peer reviewed science when developing drinking water standards. In applying these principles, "best available" usually refers to the availability at the time an assessment is made. UCMR data is the most extensive nationally representative occurrence data for perchlorate in public water systems; therefore, EPA analyzed this data and additional occurrence data in making a regulatory determination for perchlorate. However, there will be another opportunity to consider new data during development of a proposed NPDWR for perchlorate.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28811
EPA Comment Code: 3300

Comment: NRDC Response: Only Massachusetts has finalized a drinking water standard for perchlorate; California and New Jersey have not.

As noted in the Federal Register notice, one commenter incorrectly suggests that the population exposed would be capped because of regulatory limits in Massachusetts, California, and New Jersey. As a matter of fact, only Massachusetts has promulgated an MCL of 2 ppb for perchlorate in drinking water. California has set an unenforceable public health goal of 6 ppb.[FN63: California Office of Environmental Health Hazard Assessment, Public Health Goal for Perchlorate. See e.g. http://oehha.ca.gov/public_info/facts/Perchloratefacts.html.] New Jersey has proposed, but has not finalized, an enforceable standard of 5 ppb.[FN64: New Jersey Department of Environmental Protection, New Jersey Register, March 16, 2009 http://www.state.nj.us/dep//rules/notices/031609a.html]

Response: In July 2006, Massachusetts set an Maximum Contaminant Level (MCL) of 2 µg/L and in October 2007, California set an enforceable MCL of 6 µg/L. New Jersey proposed an MCL of 5 µg/L in April 2009 but has not finalized it.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Department of Environmental Protection (NJDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0527
EPA Comment ID: 28912
EPA Comment Code: 3300

Comment: Occurrence Analysis

USEPA seeks information on the occurrence of perchlorate at concentrations below the MRL of 4 ug/L in the Unregulated Contaminant Monitoring Rule (UCMR) studies. In studies conducted by NJDEP between 2003 and 2005, subsequent to UCMR sampling, the laboratory was able to achieve a MRL of 1 ug/L or lower using EPA Method 314.0. In this study, community and non-community public water systems were chosen based on their potential vulnerability to perchlorate contamination. Reasons for sampling included proximity to military installations and unexploded ordnance, and proximity to previous UCMR-tested sites that showed perchlorate detections; a few of the individual public wells that had tested high in the original UCMR sampling were sampled. Most, but not all, of these samples were taken before treatment. A small number of these were point of entry (POE) samples. Perchlorate was detected in 11 of the 67 public water systems tested at 1 ug/L or above (NJDWQI, 2005).

Response: Please see the response to comment code 3300.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group (EWG)
EPA Document ID: EPA-HQ-OW-2009-0297-0499
EPA Comment ID: 28934
EPA Comment Code: 3300

Comment: In 2005, EWG published findings from a national analysis of tap water contamination based on data provided by public water suppliers from seven states, including Texas and California (EWG 2005). In our analysis, perchlorate levels above the level of quantification were considered significant; we found that over 26 million people in these seven states were served by water systems that had at least one perchlorate detection. Since this data was gathered from only seven states, we expect that the actual number of people in all 50 states who are served by public water systems with at least one perchlorate detection would be much higher.

EWG recommends that the agency consider any perchlorate detections above the level of quantification as significant; this would give a more accurate picture of the number of U.S. residents who are actually drinking perchlorate contaminated water.

Response: Please see response to comment code 5220. Also, see response to comment code 3300.

EPA Comment Code: 4000 Evaluation of Perchlorate Exposure from Sources Other than Drinking Water

Individual Comments
Commenter Name: Peter King
Commenter Organization: American Public Works Association (APWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0156
EPA Comment ID: 20261
EPA Comment Code: 4000

Comment: Moreover, APWA supports EPA's assessment that additional investigation is necessary to ascertain total human exposure and health risks of perchlorate and MTBE before a preliminary determination may be made regarding these chemicals. Finally, we agree that it is important for the Agency to try and identify data that can be used to estimate the contribution of perchlorate exposure from food versus drinking water and we feel as though the urinary bio-monitoring approach is appropriate.

Response: EPA agrees with the commenter and has refined its urinary biomonitoring approach to apportioning perchlorate exposure between food and water.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group (PSG)
EPA Document ID: EPA-HQ-OW-2007-0068-0168
EPA Comment ID: 20280
EPA Comment Code: 4000

Comment: USE OF ALTERNATIVE APPROACHES WOULD ENABLE EPA TO MAKE A DETERMINATION ON PERCHLORATE WITH GREATER SPEED AND SCIENTIFIC CERTAINTY

In its Support Document, EPA presents a number of alternatives for evaluating the third statutory criterion, of "meaningful opportunity for health risk reduction" for perchlorate.[FN4: US EPA Regulatory Determinations Support Document for CCL2, May 2007 [hereinafter, CCL 2 Support Document].] Many of these approaches take advantage of the extensive scientific information available on perchlorate.

EPA outlines several options in its Support Document for using the superior biomonitoring data for its regulatory determination. Clearly, real-time human data can be uniquely valuable and would enable EPA to make a determination on perchlorate with greater speed and scientific certainty. Using such powerful new data, EPA can make a determination more quickly and with more scientific certainty than was possible in the past. The National Health and Nutrition Examination Survey (NHANES) biomonitoring data provides a more reliable estimate of total perchlorate exposure in the US population than the fallback of extrapolating from food data.[FN5: Benjamin C. Blount et al., Perchlorate Exposure of the US Population, 2001-2002, J. Expos. Sci. Envtl. Epidemiol., Oct. 2006 [hereinafter Blount 2006c].]

The biomonitoring data demonstrates that total perchlorate exposure from all sources is below the EPA's health benchmark for virtually all US residents. Since drinking water exposure is a small subset of total exposure, it follows that reducing this small subset by a small amount through regulation will not meet the meaningful risk reduction criterion of the Safe Drinking Water Act.

There are two additional approaches that merit Agency consideration, further suggesting that drinking water perchlorate levels pose no meaningful risk to human health. One approach posits that it is unnecessary for EPA to adjust for total exposure because Greer et al.[FN6: Monte A. Greer et al., Health Effect Assessment for Environmental Perchlorate Contamination: The Dose Response for Inhibition of Thyroidal Radioiodide Uptake in Humans, Envtl. Health Perspectives, Sep. 2002, at 927.] and other studies relied on by the NAS panel are studies of total exposure. The last approach posits that EPA could consider the comparative effect on iodine uptake inhibition (IUI) of perchlorate exposure in drinking water to other dietary goitrogens in determining whether there is meaningful opportunity for risk reduction.

In Attachment 2 [See PDF of docket ID EPA-HQ-OW-2007-0068-0168], we discuss the supplemental or alternative approaches that EPA can adopt to directly answer the question of whether regulation of perchlorate in drinking water will result in meaningful reduction in human health risk.

Response: EPA agrees that biomonitoring offers some unique advantages with this type of contaminant which is not metabolized and excreted via urine (and milk in lactating women). The limitation in the use of NHANES is it addresses ages 6 and above.

However, EPA disagrees that biomonitoring data demonstrates that total perchlorate exposure from all sources is below the EPA's health benchmark for US residents. The effect of additional perchlorate added via water in the Greer et al. study over the amounts in food and other iodine inhibitors in food was reflected in the RfD. It is unknown whether the background levels of inhibitors altered the shape of the dose response curve to either lessen or increase the dose of perchlorate required to detect iodine uptake inhibition in the subjects. We presume a straight line i.e., that regardless of the background in the subjects, the incremental additional perchlorate required was 0.07 ug/kg/day to arrive at the NOEL for the additional perchlorate. Given that this notice regards whether or not to regulate perchlorate in drinking water, allowing a normal background of goitrogens in the subjects' diets reveals the additional amount in water needed to produce inhibition. It could be argued that apportionment between food and water has already taken place since this is not total perchlorate, but added water over and above the food. Because these variables are unknown outside of a sequestration study where precise amounts of perchlorate from all food and water is measured, EPA assumes additional perchlorate from any source, food or water, produces the iodine uptake inhibition reflected by the RfD.

Regarding the comment that EPA could consider the comparative effect on iodine uptake inhibition of perchlorate exposure in drinking water to other dietary goitrogens in determining whether there is meaningful opportunity for risk reduction, EPA believes that the approach has merit; however, a cumulative risk assessment would require significant new data collection and would unnecessarily delay regulatory decision making for perchlorate. The Administrator will make regulatory determinations on a case-by-case, contaminant specific basis. In making a regulatory determination, the Administrator considers the adverse health effect of the particular contaminant at issue as well as the occurrence or likelihood of occurrence of the contaminant in public water systems with a

frequency and at levels of public health concern. Finally, it is the sole judgment of EPA's Administrator to determine whether there is a meaningful opportunity to reduce health risk for persons served by public water systems.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1724
EPA Comment ID: 20616
EPA Comment Code: 4000

Comment: After reading the EPA report, it is clear the EPA did not consider the fact that perchlorate is concentrated many times (19X was cited) in lettuce, which is watered in California by perchlorate contaminated water. Studies of perchlorate concentrations in lettuce found in supermarkets across the US finds high concentrations of perchlorate in lettuce, which is usually grown in California. The EPA study did not utilize this information in its findings. Until the EPA allows this information into its deliberations, their study, and findings, are not complete. DOD has effectively blocked the lettuce findings, and President Bush has refused to allow the EPA to conduct further studies, saying we are at war, which protects DOD from the costs of clean-up. If the reader would consider his or her own family, women would probably be found taking Synthroid due to thyroid issues. Might the fact that women tend to eat more salads than men correlate? None of these issues are addressed by the EPA.

Response: Leafy vegetables do concentrate salts such as perchlorate as water evaporates from leaves (evapotranspiration). EPA has evaluated early studies of perchlorate content of food and reported these findings in the May 1, 2007 Federal Register notice. The data from FDA's total diet study as well as biomonitoring studies by EPA/CDC have further refined the contribution of food to perchlorate exposure in various age/sex groups as discussed in the October 10, 2008 and August 19, 2009 notices. EPA does not believe that the widespread presence of perchlorate in food overrides the need for public health risk reduction for persons served by PWSs with perchlorate contamination. EPA recognizes that a drinking water regulation would not eliminate total perchlorate exposure, but believes that the reduction in perchlorate exposure in drinking water presents a meaningful opportunity for health risk reduction for persons served by PWSs contaminated by perchlorate.

Commenter Name: Apparent Mass Mailing #6 - Earth Justice
EPA Document ID: EPA-HQ-OW-2008-0692-0972
EPA Comment ID: 20886
EPA Comment Code: 4000

Comment: EPA's analysis fails to consider that the combination of food and drinking water exposure to perchlorate in the U.S. population exceeds the reference dose set by EPA. Nor does it incorporate the more protective methodology behind the recent state regulatory actions. These flaws must be remedied for the sake of the millions of U.S. families exposed to dangerous levels of perchlorate contamination.

Response: EPA considers the combination of food and drinking water through the relative source contribution (RSC). The RSC is the percentage of the reference dose remaining for drinking water

after other sources of exposure to perchlorate have been considered (e.g., food). See the August 2009 Federal Register notice (41887) for a detailed discussion of RSC derivation.

Regarding the comment about incorporating methodologies behind recent state regulatory actions, States use different methodologies or assumptions to derive their own standard based on their unique exposure scenarios. EPA has used the best available peer reviewed science in making this regulatory determination.

EPA Comment Code: 4110 Dietary studies – FDA's 2005-2006 total dietary study (TDS)

Individual Comments
Commenter Name:
Commenter Organization: Ag Council et al
EPA Document ID: EPA-HQ-OW-2008-0692-1987
EPA Comment ID: 20976
EPA Comment Code: 4110

Comment: FDA's Food Sampling Results Reveal that Perchlorate Concentrations are Below the Level of Concern and that Iodine intake Actually Exceeded NAS-Recommended Levels for all Groups Across the US Population.

When perchlorate was first discovered in food, the FDA began sampling produce and bottled water in an effort to characterize perchlorate occurrence in food. FDA later expanded its perchlorate sampling effort to include other vegetables, fruits and milk to gain a greater understanding of the range of foods that contain perchlorate. FDA's efforts included a total dietary survey (TDS), the results of which were provided to US EPA for use in determining total perchlorate exposure in the US population.

TDS is a market basket survey of various foods analyzed for perchlorate and iodine, conducted by FDA from 2003-2006. In early 2008, FDA published its testing results for 285 food samples in each of three cities in each of the four regions of the country. FDA evaluated the food data based upon estimated food consumption patterns of 14 age/sex groups from 6-11 month-old infants up to 70+ year-old men and women.

FDA found that the average daily intake of perchlorate was well below both the NAS RfD and health reference level (HRL). FDA identified children 2 years of age as having the highest average intake of perchlorate at 0.35 to 0.39 ug/kg bw/day, which at the upper end is slightly more than half of the RfD, but still below the HRL.

For iodine, FDA found that each of the 14 age/sex groups, including infants, children, and women of childbearing age exceeded the average intake levels estimated by the NAS to meet requirements for healthy individuals.

In light of these findings, FDA continues to stand by its prior recommendation that consumers should not alter their infants' and children's diets and eating habits. Indeed, many of the foods at issue are major dietary sources of iodine and other nutritionally essential substances.

Response: No response necessary to this summary of FDA TDS information.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21065
EPA Comment Code: 4110

Comment: iii. Murray et al. (2008)

The Food and Drug Administration (FDA) total diet study (TDS) was "designed to monitor the U.S. food supply for chemical contaminants, nutritional elements, and toxic elements." Based on measurements of perchlorate and iodine in market baskets, the Murray et al. report estimated intake doses. The sampling approach is based on "market baskets" that are collected four times per year. Each market basket contains 285 foods, collected simultaneously in three cities within a region. The modeled group estimated to have the greatest dietary exposure to perchlorate was children age 2 (0.35 to 0.39 ug/kg-day). This is due to the high intake of dairy products coupled with low body weight. The modeled dose for the most sensitive population, the fetuses of pregnant women, was not specifically modeled, but the estimated dose for women of child bearing age was 0.09 to 0.11 ug/kg-d.[FN3: The estimated doses for women ages 14-16, 25-30, and 40-45 were all 0.09 to 0.11 ug/kg-d.] Adult men age 25 to 30 years old were estimated to be exposed to 0.08 to 0.11 ug/kg-day. Of the foods measured in this study, spinach, tomatoes, and cantaloupe had the highest levels of perchlorate at 40, 78, and 24.4 ug perchlorate/kg wet weight of food, respectively.

This study can be used to estimate exposures to perchlorate based on actual food concentrations. Even at the highest estimate, this dose was less than the U.S. EPA RfD of 0.7 ug/kg-day. The study does not aim to evaluate overall body steady-state serum concentrations of perchlorate, only dose. Children age 2 have a higher renal excretion rate than adults or infants do, which would reduce their steady-state serum concentration despite the higher intake.[FN4: Perchlorate is a non-metabolized pharmaceutical agent with nearly complete urinary excretion. Data on adult and child clearances is available for other pharmaceuticals making it possible to extrapolate the rate of a child's clearance of perchlorate compared to an adult's. Based on the clearance of gabapentin, gentamicin, isepamicin, ticarcillin, and vancomycin, the clearance in a child is 1.6 times that of an adult (unpublished data).]

Response: EPA does not believe that the widespread presence of perchlorate in food overrides the need for public health risk reduction for persons served by PWSs with perchlorate contamination. The Agency presented an extensive evaluation of dietary exposure to perchlorate in the October 2008 and August 2009 notices (73 FR 60262; USEPA 2008a and 74 FR 41883; USEPA 2009b). EPA has used this dietary exposure data to account for the relative source contribution (RSC) of perchlorate from food. EPA recognizes that a drinking water regulation would not eliminate total perchlorate exposure, but believes that the reduction in perchlorate exposure in drinking water presents a meaningful opportunity for health risk reduction for persons served by PWSs contaminated by perchlorate. Please see response to comment code 5220 for a discussion of EPA's revised approach to deriving potential HRLs.

Commenter Name: Sonia Salas
Commenter Organization: Western Growers Association on behalf of several California agriculture groups
EPA Document ID: EPA-HQ-OW-2009-0297-0652
EPA Comment ID: 28679
EPA Comment Code: 4110

Comment: US FDA's Food Sampling Results Reveal that Perchlorate Concentrations are Below any Meaningful Level of Concern and that Iodine Intake Actually Exceeds NAS- Recommended Levels for all Groups Across the US Population.

When perchlorate was first discovered in food, the U.S. FDA began sampling produce and bottled water in an effort to characterize perchlorate occurrence in food. FDA later expanded its perchlorate sampling program to include other vegetables, fruits and milk to gain a greater understanding of the range of foods containing perchlorate. FDA's work included a total dietary survey (TDS), the results of which were provided to US EPA for use in determining total perchlorate exposure in the US population.

The Total Dietary Survey is a market basket survey of various foods analyzed for perchlorate and iodine, conducted by FDA from 2003-2006. In early 2008, FDA published its testing results for 285 food samples in each of three cities in each of the four regions of the country. FDA evaluated the food data based upon estimated food consumption patterns of 14 age/sex groups from 6-11 month-old infants up to 70+ year-old men and women.

FDA found that the average daily intake of perchlorate was well below both the NAS' recommended RfD and USEPA's current 15 ppb health reference level (HRL). FDA identified children 2 years of age as having the highest average intake of perchlorate at 0.35 to 0.39 ug/kg body weight/day, which at the upper end is slightly more than half of the RfD, but still below the HRL.

Response: In the October 2008 preliminary regulatory determination, EPA had derived a single HRL of 15 µg/L based upon the RfD, an estimate of perchlorate exposure from food for pregnant women, and traditional adult body weight (70 kg) and drinking water consumption (2 L/day) values. This single HRL was derived to reflect exposure to a pregnant woman and her fetus, which the NRC identified as "the most sensitive population." Since the NRC also identified infants and developing children as additional life stages, EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 µg/L to 47 µg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These HRLs are calculated based on individuals who consume an average amount of perchlorate from food (except for pregnant women where EPA used a 90th percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts. EPA is evaluating these potential alternative HRLs and considers them to be levels of public health concern for purposes of this determination.

Commenter Name: Sonia Salas
Commenter Organization: Western Growers Association on behalf of several California agriculture groups
EPA Document ID: EPA-HQ-OW-2009-0297-0652
EPA Comment ID: 28680
EPA Comment Code: 4110

Comment: These results, taken together with the results of EPA's 2006 tests of nearly 40,000 water samples from across the U.S.,[FN1: Office of Water: The Analysis of Occurrence Data from the First Unregulated Contaminant Monitoring Regulation (UCMR1) in support of Regulatory Determinations for the Second Drinking Water Contaminant Candidate List (EPA 815-D-06-008);] which show that perchorate levels were less than seven parts per billion in 99% of the samples, provide no evidence that individuals ingest perchlorate at daily doses exceeding the Reference Dose.

They also suggest that there is little likelihood that such exposures would occur. This conclusion is further supported by data from the U.S. Centers for Diseases Control's National Health and Nutrition Examination Survey (NHANES) biomonitoring dataset (see below).

Response: Since the NRC also identified infants and developing children as additional life stages, EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 µg/L to 47 µg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These HRLs are calculated based on individuals who consume an average amount of perchlorate from food (except for pregnant women where EPA used a 90th percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts. EPA is evaluating these potential alternative HRLs and considers them to be levels of public health concern for purposes of this determination. The CDC NHANES biomonitoring data set does not include data for all life stages.

EPA Comment Code: 4130 Dietary studies -- other studies, models, and data (besides FDA's 2005-2006 TDS, and 2003-2005 exploratory data)

Individual Comments
Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group (PSG)
EPA Document ID: EPA-HQ-OW-2007-0068-0170
EPA Comment ID: 20289
EPA Comment Code: 4130

Comment: July 24, 2007 US Environmental Protection Agency Office of Water Docket (Mailcode 2822T) 1200 Pennsylvania Avenue, NW Washington, DC 20460

RE: Supplemental Comments on Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List Rule, Docket ID: EPA-HQ- OW-2007-0068

In May 2007, the US Food and Drug Administration posted a Preliminary Estimation of Perchlorate Dietary Exposure Based on FDA 2004/2005 Exploratory Data on the web at www.cfsan.fda.gov/~news/whatsnew.html. Perchlorate exposure from consumption of 27 foods and beverages was estimated via a Monte Carlo simulation. The Monte Carlo simulation sums perchlorate exposure values based on food intake and perchlorate concentration levels randomly drawn from a range of possible values for each food from a particular iteration to yield a total exposure for an individual. The summary of their analysis is presented in their Table as follows:

[Table. Summary of Population-Based Perchlorate Exposures]

FDA did not consider other dietary goitrogens such as nitrate and thiocyanate in their analysis in order to place these results in perspective. Although thiocyanate is the most significant dietary goitrogen that shares the same mechanism of action as perchlorate, the food content of thiocyanate precursors is not widely reported. On the other hand, the nitrate contents of various dietary sources has been widely reported in the peer reviewed literature and nitrate is known to share the same mechanism of action as perchlorate (competitive inhibition of iodine uptake by the thyroid). Nitrate is known to be approximately 1/240th as potent as perchlorate on a weight ingested basis in the inhibition of iodide uptake (IUI). (Tonacchera et al., 2004)

Due to the data gap, the Perchorate Study Group (PSG) contracted with Kenny Crump and Cynthia Van Landingham of Environ in Ruston, LA to perform a similar Monte Carlo analysis of nitrate consumption to assess the relative importance of these two dietary goitrogens on IUI [See PDF of docket ID EPA-HQ- OW-2007-0168-0170]. Using the relative potencies of nitrate and perchlorate derived from Tonacchera, the nitrate data summaries from Crump & Van Landingham, Table 4 can be compared directly with the perchlorate summaries from FDA in their Table 2. These comparisons are presented below.

[Table 2 See PDF of docket ID EPA-HQ-OW-2007-0168-0170]

Thus, this analysis indicates that dietary nitrate is two to three orders of magnitude more significant than dietary perchlorate in IUI by the thyroid. Controlling dietary perchlorate is thus relatively insignificant to overall thyroid health than is controlling dietary nitrate intake.

Thank you for allowing us the opportunity to submit this supplemental information for consideration by the Agency in making a regulatory determination on perchlorate.

Sincerely, Michael Girard The Perchlorate Study Group

Attach:

[Attachment - see PDF]

Response: EPA considers the combination of food and drinking water through the relative source contribution (RSC). The RSC is the percentage of the reference dose remaining for drinking water after other sources of exposure to perchlorate have been considered (e.g., food). See the August 2009 Federal Register notice (74 FR 41883; USEPA 2009b) for a detailed discussion of RSC derivation. EPA acknowledges that nitrate and thiocyanate have the same mode of action as perchlorate, and that the effects of combined exposure to perchlorate, nitrate, and thiocyanate are additive, EPA does not believe there are sufficient scientific data currently available to assess and characterize the combined risk of these contaminants. EPA has committed to a drinking water strategy that outlines four principles to expand public health protection for drinking water (USEPA, 2010b). One of these principles is to address contaminants as groups. However, EPA does not believe that regulatory action to address perchlorate should be further delayed. Therefore, EPA intends to develop a proposed rule for perchlorate. At such time as a NPDWR is promulgated, EPA is required to review and revise, as appropriate, its drinking water standards at least every six years. Any revision must at least maintain or improve public health protection. When there are sufficient scientific data to assess the cumulative risks of perchlorate and other contaminants, EPA will review this information to evaluate whether any new or revised NPDWRs are appropriate.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association
EPA Document ID: EPA-HQ-OW-2008-0692-1424
EPA Comment ID: 20440
EPA Comment Code: 4130

Comment: Since the NRC published its findings in 2005, several studies have been completed that provide data necessary to evaluate; the, population exposure potential. In the study developed by Mendez et.al. (2008), probabilistic (Monte Carlo) simulation was used to estimate the potential contribution of drinking water to the aggregate perchlorate intake by the presumed most sensitive population, reproductive age women. The full report is attached as Appendix A [see PDF Docket ID EPA-HQ-OW-2008-0692-1424] to these comments. Food perchlorate concentration distributions were derived from the FDA 2004-5 Exploratory Sampling dataset. Food and waterconsumption data were obtained from the USDA Continuing Survey of Food Intake by Individuals (CSFII) from 1994-96 and 1998. The Monte Carlo simulation derives three distributions of perchlorate concentrations in drinking water, corresponding to "raw" data from EPA's UCMR1 national perchlorate sampling, data from the UCMR1 with low-level "background" perchlorate concentrations added to a portion of the entry points below detection limits, and UCMR1 data for

large California systems, again with "background" perchlorate concentrations added to a proportion of non-detect observations.

Inclusion of the estimated national drinking water distributions in the simulation resulted in increases in estimated median perchlorate intakes 3-20 percent greater than those seen when only dietary sources were evaluated. The perchlorate intake distributions estimated based on diet and water intake were found to be very similar to the distributions estimated based on perchlorate excretion data from 2001-2002 and 2003-2004 National Health and Nutrition Examination Survey (NHANES) data sets. The intake estimates based on diet and water and estimates derived from urinary excretion analyses suggestthat approximately two to five percent of reproductive age women in the U.S. receive perchlorate intake greater than 2x10-4 mg/kg-day, which is approximately one-third of the RfD for perchlorate. This proportion does not appear to be strongly affected by reasonable assumptions related to background drinking water contamination. The proportion of women with intakes above the RfD (7x10-4 mg/kg- day) cannot be estimated accurately from either the dietary intake analysis or NHANES data because of the sparcity of data in the upper percentiles of the distribution, but is likely to be considerably lower than two percent nationally. In addition, the proportion of women adversely effected by perchlorate exposure is likely to be even lower, since perchlorate appears to adversely effect thyroid function only in women with insufficient iodine intake. (Blountet al. 1996).

This finding, that the total dietary exposure (food and drinking water) of reproductive age women in the U.S. is approximately one-third of the RfD for perchlorate at the 95th percentile, is complimentary to the finding referenced in the proposed decision based on a joint assessment prepared by EPA-CDC. Given this evidence related to limited exposure potentials and estimated intakes well below the RfD it is clear there is limited potential for perchlorate to present a significant adverse affect on the nation's health, including sensitive subpopulations.

Response: EPA disagrees and has decided to regulate perchlorate in drinking water. See response to comment code 6120. EPA estimates that at least 5.1 to 16.6 million people are served by PWSs, for which we have data, that have perchlorate contamination. EPA has determined that a NPDWR for perchlorate could reduce perchlorate exposures for these populations to levels below the potential alternative HRLs that EPA has identified as levels of public health concerns for purposes of this determination, and that such exposure reductions present a meaningful opportunity for the reduction of health risks for persons served by PWSs.

Commenter Name: Kathy Curtis
Commenter Organization: Alliance of Nurses for Healthy Environments (ANHE)
EPA Document ID: EPA-HQ-OW-2009-0297-0651
EPA Comment ID: 28545
EPA Comment Code: 4130

Comment: EPA must also consider other exposure pathways and additional contaminants in the environment that impact thyroid function when establishing the MCL. Studies of perchlorate levels in food, including breast milk, show that the population is exposed through multiple pathways in addition to contaminated drinking water.

Response: See response to comment ID 20289 under comment code 4130. Additionally, EPA does apportion the exposure to perchlorate to food and derived the drinking water allowance considering the portion of the RfD already used by food.

Commenter Name: Robert E. Brackett
Commenter Organization: Grocery Manufacturers Association (GMA)
EPA Document ID: EPA-HQ-OW-2009-0297-0413
EPA Comment ID: 28706
EPA Comment Code: 4130

Comment: GMA is concerned that Environmental Protection Agency's (EPA) approach to assessing potential risks of perchlorate in drinking water will be widely misunderstood and misinterpreted, leading to confusion and unnecessary concern among US consumers, and food importers, global policy makers, and regulatory bodies about perchlorate in US food products. GMA believes that sound public health policy requires that the relevant government agencies, including EPA, send a clear and consistent message to consumers that any hypothetical risks of perchlorate exposure to pregnant women and mothers of infants estimated by EPA are easily avoided by eating iodine-rich foods or taking an iodine supplement. This approach confers the double benefit of decreasing risk of disease associated with inadequate iodine intake as well as mitigating any potential risks of environmental exposure to perchlorate. We will elaborate below.

First, it is important for EPA to be clear with the public that exposure to perchlorate, or to other substances in the diet that may interfere with iodine uptake by the thyroid, is only a potential problem in individuals with iodine deficiency. There is no evidence that iodine deficiency is currently a serious situation in the United States.[FN1: FDA has estimated iodine intake by the US population using data from the Agency's Total Diet Study (http://www/fda.gov/Food/FoodSafety/FoodContaminantsAdulteration/ChemicalContaminants/Perchlorate/ucm077572.htm)]

Based upon common food consumption patterns in the United States, and the availability of iodine within the US diet, only those individuals consuming highly restrictive diets or those deliberately avoiding iodine are at high risk of deficiency. In addition to naturally rich sources of iodine, such as fish and shellfish, iodine can be found in meat, poultry, and dairy products as well as in many manufactured food items including cereals and baked goods. Further, table salt is frequently consumed in an iodized form. Many dietary supplements, including prenatal multivitamin and mineral supplements contain iodine.[FN2: C Fields, M Dourson, J Borak. Iodine-deficient vegetarians: a hypothetical perchlorate-susceptible population? Regulatory Toxicology and Pharmacology 42 (2005):37-46] Despite the fact that data from NHANES I and NHANES III surveys suggested a decline in iodine consumption, data from more recent NHANES analyses show that iodine consumption has stabilized to a median level considered adequate based upon the World Health Organization guidelines for population adequacy.[FN3: KL Caldwell, R Jones, JG Hollowell. Urinary Iodine Concentration: United National Health and Nutrition Examination Survey 2001-2002. Thyroid 15(7) 2005: 692-699] The Institute of Medicine's Food and Nutrition Board Dietary Reference Intake report for iodine concluded that infants under six months of age fed a diet exclusively of breastmilk have adequate and appropriate intake levels to support normal growth and development.[FN4: http://www.nap.edu/catalog.php?record_id=10026] In addition, infant formula manufacturers are required to fortify infant formula sold in the United States with iodine based

upon the Food and Drug Administration's (FDA) infant formula composition regulations found at 21 CFR 107.

There is no evidence of pervasive iodine deficiency in the United States in infants, children or adults. Some populations are hypothetically more at risk for effects of perchlorate consumption, most notably women of child-bearing age and pregnant women. Because of inadequate iodine consumption during pregnancy can lead to negative birth outcomes, any further reduction uptake by the thyroid from exposure to perchlorate could pose a risk. However, there is no evidence of widespread iodine deficiency among women of childbearing age or pregnant women in the United States. Therefore, any potentially susceptible subpopulation could be targeted with interventions such as education about diet during pregnancy and food sources of iodine, or supplementation. Adequate prenatal care should include an evaluation of a women's diet to assess for potential micronutrient deficiencies and appropriate counseling to help women plan their diets to address their changing nutrient needs during pregnancy should be provided.

Response: EPA agrees that promoting iodide nutrition is good public health policy and may have a positive influence in reducing the iodide uptake inhibition effects associated with exposure to perchlorate. However, the Agency does not think it is appropriate to rely on the promotion of iodide nutrition in this case, especially since these activities are outside of EPA's SDWA authority. The three SDWA criteria for a positive regulatory determination have been satisfied. While the health concerns associated with perchlorate may be addressed through other means, it is the Administrator's judgment that a standard limiting perchlorate in drinking water can reduce health risk, particularly to fetuses, infants and children.

Commenter Name: Robert E. Brackett
Commenter Organization: Grocery Manufacturers Association (GMA)
EPA Document ID: EPA-HQ-OW-2009-0297-0413
EPA Comment ID: 28708
EPA Comment Code: 4130

Comment: GMA notes with interest the draft review of the EPA perchlorate assessment by the EPA Office of Inspector General (OIG draft)[FN5: http://www.epa.gov/oig/reports/2009/20081230-2008-0010.pdf]. The OIG draft points out that there are other compounds occurring naturally in foods that act in similar ways as perchlorate, and that regulating the perchlorate level in drinking water is therefore unlikely to make any material difference. The best way to protect public health would be to assure that the iodine status of sensitive subpopulations is adequate. As discussed above, there is no evidence that the iodine status of sensitive subpopulations is inadequate, we agree with OIG that promoting adequate iodine intake by the population appears to be a superior approach to regulating perchlorate as a contaminant in public drinking water systems.

Third, GMA is concerned that EPA's approach to assessing potential risks of perchlorate in drinking water will lead to confusion and unnecessary concern among importers of US food products about the potential for perchlorate in commodities and food products exported by the United States. FDA has reported finding perchlorate in targeted monitoring of some foods, and continues to test additional food types for perchlorate to further enhance the assessment of dietary exposure to consumers. EPA's concern is manmade sources of perchlorate, but perchlorate is known to form in the atmosphere and to occur naturally in the environment, notably in certain geographic deposits

mined for fertilizer, the safety of perchlorate in food is scheduled for thorough evaluation on an international basis by the Joint FAO-WHO Expert Committee on Food Additives and Contaminants (JECFA) in 2010.[FN6: Tolerable Daily Intakes (TDIs) established by JECFA form the basis for food standards and maximum residue limits (MRLs) in foods established by the Codex Alimentarius Commission (Codex). Codex was created in 1963 by FAO and WHO to develop food standards, guidelines and related texts such as codes of practice under the Joint FAO/WHO Food Standards Programme. The main purposes of this Programme are protecting health of the consumers and ensuring fair trade practices in the food trade, and promoting coordination of all food standards work undertaken by international governmental and non-governmental organizations (http://www.codexalimentarius.net/web/index_en.jsp).]

In summary, we reiterate that sound public health policy requires the relevant government agencies, including EPA, to send a clear and consistent message to consumers. Any hypothetical risks of perchlorate exposure to pregnant women and mothers of infants as estimated by EPA are easily avoided by eating iodine-rich foods or taking an iodine supplement. This approach will not only mitigate any risk that may be associated with environmental exposure to perchlorate, but will also decrease the risk of disease associated with inadequate iodine intake.

GMA appreciates this opportunity to provide comments on EPA's approaches to the interpretation of the scientific data relevant to a regulatory determination for perchlorate in drinking water. We urge EPA to work in concert with FDA to assure that consumers are given balanced and consistent advice and perspective concerning the theoretical risks of chemical exposures, including risks to sensitive subpopulations. Providing this balance and perspective is particularly critical in the case of chemicals that may occur in foods that are sources of essential nutrients conferring substantial overall net benefits to health.

Sincerely yours, Robert E. Brackett, Ph.D. Senior Vice President and Chief Science and Regulatory Affairs Officer

Response: See response comment ID 28706 under comment code 4130.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group (EWG)
EPA Document ID: EPA-HQ-OW-2009-0297-0499
EPA Comment ID: 28932
EPA Comment Code: 4130

Comment: EWG supports the agency's decision to develop HRLs based on life stage and drinking water ingestion rates but we would like to bring attention to some findings from a recent CDC study of infant formula contamination that we believe would change the HRLs for infants six months of age and under. In this study, researchers tested 15 brands of powdered infant formula for perchlorate and found contamination in every brand; the two most contaminated brands, made from cow's milk, accounted for 87 percent of the U.S. powdered formula market in 2000 (Schier et al 2009).

In Table 4 of the CDC study, the researchers estimate the minimum water perchlorate concentration needed to reach the current RfD for infants at one month and six months of age at different body weight percentiles. At the highest perchlorate concentration found in the formula samples (5.05

ug/l), the researchers found the estimated minimum water perchlorate concentration needed to reach the RfD was zero for the following four exposure scenarios:

- One month old infant, 10th percentile body weight - One month old infant, 50th percentile body weight - One month old infant, 90th percentile body weight - Six month old infant, 90th percentile body weight

In fact, in all four of these exposure scenarios, infants would exceed the current RfD from formula consumption even with perchlorate levels at zero in the water used to reconstitute it. A recent GAO report found that by six months of age, less than 30% of infants are exclusively breast-fed (GAO 2006); in addition, powdered infant formulas account for 50 to 60% of the total infant formula market. This means that millions of infants per year may be exposed to powdered infant formula that is so heavily contaminated with perchlorate that formula exposures alone in these infants may exceed the current RfD.

These results suggest that for infants six months of age and younger who are fed powdered formula, there is no safe HRL since any can of powdered formula may be contaminated with perchlorate at high enough concentrations that formula consumption alone results in exposures above the RfD. EWG recommends that the agency incorporate these exposure dosing scenarios from the formula study and modify the HRLs for infants six months and younger to reflect these findings.

Response: EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 µg/L to 47 µg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These HRLs are calculated based on individuals who consume an average amount of perchlorate from food (except for pregnant women where EPA used a 90th percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts. EPA is evaluating these potential alternative HRLs and considers them to be levels of public health concern for purposes of this determination.

EPA Comment Code: 4210 Biomonitoring -- urinary data from the 2001-2002 NHANES study, and EPA/CDC's NHANES-UCMR analysis

Individual Comments
Commenter Name: Gregg Grunenfelder
Commenter Organization: Washington State Department of Health; and Oregon Department of Human Services
EPA Document ID: EPA-HQ-OW-2008-0692-1529
EPA Comment ID: 20456
EPA Comment Code: 4210

Comment: Blount, et al. [FN12: Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, and Caldwell KL. 2006. Urinary Perchlorate and Thyroid Hormone Levels in Adolescent and Adult Men and Women Living in the United States. Environmental Health Perspectives (114)12: 1865-71.] evaluated 2001-2002 biomonitoring results from the National Health and Nutrition Examination Survey (NHANES) looking at urinary perchlorate, urinary iodine, and thyroid hormone levels and determined that total thyroxine (T4) and thyroid stimulating hormone (TSH) levels were related to urinary perchlorate in women. TSH and T4 levels were used as indicators of how well the thyroid was functioning. TSH causes the thyroid gland to produce triiodothyronine (T3) and T4. Both hormones are needed for normal brain development. Perchlorate was a significant positive predictor of TSH in women with urinary iodine >100 ug/l and significant positive predictor of TSH and negative predictor of T4 in women with low urinary iodine (< 100 ug/l). This implies that women and fetuses of women with low dietary intake of iodine can be impacted by perchlorate at current exposure levels in the United States population. This is especially of concern because recent NHANES data show that nearly 17% of reproductive aged women in the United States have urinary iodine levels less than 50 ug/l. The World Health Organization classifies someone as being iodine deficient at a urinary iodine level below 100 ug/l.

Response: EPA agrees that low iodide nutritional status increases the likelihood of negative impacts due to perchlorate.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20906
EPA Comment Code: 4210

Comment: * EPA presents results from an unpublished study and relies on this study to justify a HRL of 15 ug/L (ppb) for perchlorate in drinking water, although this study does not look at risks to young children or breast-fed infants;

Response: In the October 2008 preliminary regulatory determination, EPA had derived a single HRL of 15 µg/L based upon the RfD, an estimate of perchlorate exposure from food for pregnant women, and traditional adult body weight (70 kg) and drinking water consumption (2 L/day) values. This single HRL was derived to reflect exposure to a pregnant woman and her fetus, which the NRC identified as "the most sensitive population." The study supporting this HRL was made available to the public through the regulations.gov web site and was peer reviewed outside the

Agency. The study focused on the most sensitive life stage available in the data (biomonitoring data are not available for children under the age of 6).

In the August 9, 2009, notice (74 FR 41883; USEPA 2009b), EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information. These potential alternative HRLs are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These potential alternative HRLs are calculated based on individuals who consume an average amount of perchlorate from food (except for pregnant women where EPA used a 90th percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts.

EPA is evaluating these potential alternative HRLs and considers them to be levels of public health concern for purposes of this determination.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20914
EPA Comment Code: 4210

Comment: EPA presents new information from unpublished study that does not include young children: In its assessment, EPA presents an unpublished study in which EPA and CDC researchers merged urine perchlorate levels from the NHANES study and water contamination data from the Unregulated Contaminants Monitoring Regulation with the goal being to "derive the dose of perchlorate coming from food alone by eliminating possible sources of water contribution" (EPA 2008). Individuals from the NHANES study were categorized into three groups depending on whether the counties in which they resided were found to have drinking water contaminated with perchlorate or not. Using this approach, EPA was able to estimate daily perchlorate intakes for those with likely perchlorate exposure through drinking water and those without; EPA concluded that "The mean total exposure for people that are more likely to be exposed to perchlorate in food and water was calculated to be 0.101 ug/kg/day. The average exposure for people more likely to be exposed to perchlorate from food alone was 0.090 ug/kg/day" (EPA 2008).

This approach allows EPA to estimate that the population they consider to be most at risk, pregnant women and the developing fetus, can be exposed to perchlorate levels in drinking water as high as 15 ug/L and still not exceed the RfD. The most glaring flaw with EPA's study is that it does not include young children. The FDA research establishes that young children have the highest perchlorate exposures from food and therefore, are most likely to exceed EPA's RfD from additional exposures to contaminated drinking water. The NHANES data does not include information on children under the age of 6 so EPA's study using NHANES data has an enormous data gap which basically invalidates the findings from this study.

Response:
EPA believes that the UCMR-NHANES data merge is valid for the age groups that were represented. The study was peer reviewed outside the Agency and made available to the public through the Regulations.gov web site. EPA has incorporated analyses of these life stages less than

six years of age in the 2009 August Federal Register Notice using data from FDA Total Diet Study to estimate dietary exposure.

Commenter Name: Matt Lewis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2116
EPA Comment ID: 21966
EPA Comment Code: 4210

Comment: Perchlorate can cause massive problems to growth, health, and development of children. A study by the Centers for Disease Control detected perchlorate in one out of 2,820 people. The sources for these contaminations range from Food to Groundwater to Breast Milk. The Food and Drug Administration found perchlorate in 74% of all foods tested. Future Generations will face mental retardation, loss of hearing, and deficits in motor skills if further contamination continues.

Response: EPA has decided to regulate perchlorate in drinking water. See response to comment code 6120. Also see response to comment ID 20886 under comment code 4000 for a discussion of how EPA considered exposure to perchlorate from food.

Commenter Name: Tina Carroll
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2189
EPA Comment ID: 22381
EPA Comment Code: 4210

Comment: According to your own website, ?Tests of drinking water at APG have detected perchlorate in four production wells and in the finished water supply for the city of Aberdeen.? Additionally, in 2004/2005 exploratory surveys, the FDA found ranging perchlorate levels in raw milk in Maryland.

Response: EPA has decided to regulate perchlorate in drinking water. See response to comment code 6120. Also see response to comment ID 20886 under comment code 4000 for a discussion of how EPA considered exposure to perchlorate from food.

Commenter Name: Brenda Lewis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2191
EPA Comment ID: 22391
EPA Comment Code: 4210

Comment: Perchlorate can cause massive problems to growth, health, and development of children. A study by the Centers for Disease Control detected perchlorate in one out of 2,820 people. The sources for these contaminations range from Food to Groundwater to Breast Milk. The Food and Drug Administration found perchlorate in 74% of all foods tested. Future Generations will face mental retardation, loss of hearing, and deficits in motor skills if further contamination continues.

Response: EPA has decided to regulate perchlorate in drinking water. See response to comment code 6120. Also see response to comment ID 20886 under comment code 4000 for a discussion of how EPA considered exposure to perchlorate from food.

Commenter Name: Richard M. Peekema
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0419
EPA Comment ID: 28684
EPA Comment Code: 4210

Comment: Comment on EPA-HQ-OW-2009-0297

This document gives a detailed review made earlier of the 2006 CDC urinary analysis data. That review raised questions that are still relevant to the discussion of MCL levels for drinking water. In the pages that follow, a number of conclusions can be reached.

SUMMARY AND CONCLUSIONS

1. Perchlorate was detected and quantified in the urine of all 2820 samples tested with a new analytical technique. 50% of those samples exceeded the 4 ppb median value, and 10% of those samples exceeded 10 ppb. That urinary perchlorate could not be explained as coming from water but instead being continually re- supplied by the food being eaten.

2. The correlation of the thyroid T4 hormone with urinary perchlorate as reported by Blount et al. could not be repeated exactly because the sample elimination criteria were insufficiently detailed. A least squares fit to all the data showed less correlation than Blount reported. The scatter plot of the data being correlated deserves as much consideration as correlation coefficients and relevance numbers reported by the statistical analysis. A search for a similar correlation between T4 and nitrate proved negative.

3. Iodide deficiency in women of child bearing age appears to define the population at greatest risk to perchlorate in the drinking water. The percentage of such women appears to be increasing over time, presumably from reduced iodized salt intake being invoked by personal dietary responses to public clamor over excessive salt. A water contaminant specification based on a population that has other means to control its risk but fails to do so is also not appropriate.

4. The effects of thiocyanate and nitrate cannot be ignored. But the levels of those ions in the population at risk also change with time. Reduced smoking in the population, and better control of nitrate runoff into drinking water aquifers will change the effect of those ions over time. Like the changing iodide deficiency over time, it is inappropriate to regulate a contaminant level that will change as the population at risk changes. The conclusions of the OIG report are endorsed.

Respectfully submitted, Richard M. Peekema, retired chemist San Jose, CA

Response: EPA will consider the best available data in evaluating the potential effects of perchlorate and exposure to the public. This includes the study by Blount and others that described their analysis of NHANES data. The findings and limitations of this study have been described in previous federal register notices concerning perchlorate in drinking water.

EPA agrees that perchlorate exposure may result from both food and drinking water. Previous analyses have estimated the portion of the perchlorate exposure from food. EPA considered the portion of perchlorate exposure from food in developing the potential alternative HRLs. See responses to comment IDs 20616 and 20886 under comment code 4000.
Analyses performed by Blount et al. depend upon weighting of subjects with respect to their representation for the population. Without application of appropriate weighting, the analysis cannot be properly reproduced.
EPA agrees that data indicate an increase in the number of women exhibiting low iodide status. However, this is only one of a variety of factors that will be considered in determining whether a NPDWR for perchlorate is warranted. Additional consideration of exposure and developmental stage will also be important factors to evaluate as EPA develops the proposed NPDWR.
EPA received a number of comments that the Agency should consider the comparative effect on iodine uptake of perchlorate exposure in drinking water to nitrate and thiocyanate exposure in drinking water in determining whether there is a meaningful opportunity for risk reduction. EPA's Office of Inspector General (USEPA, 2008c) believes that a NPDWR for a group of chemicals may be appropriate based on a yet-to-be-conducted cumulative risk assessment that assesses and characterizes the combined human health risk from perchlorate, nitrate, and thiocyanate.
While EPA acknowledges that nitrate and thiocyanate have the same mode of action as perchlorate, and that the effects of combined exposure to perchlorate, nitrate, and thiocyanate are additive, EPA does not believe there are sufficient scientific data currently available to assess and characterize the combined risk of these contaminants. EPA has committed to a drinking water strategy that outlines four principles to expand public health protection for drinking water (USEPA, 2010b). One of these principles is to address contaminants as groups. However, EPA does not believe that regulatory action to address perchlorate should be further delayed. Therefore, EPA intends to develop a proposed rule for perchlorate.

Commenter Name: Richard M. Peekema
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0419
EPA Comment ID: 28685
EPA Comment Code: 4210

Comment: CDC URINE PERCHLORATE ANALYSES

In 2006 the US Center for Disease Control (CDC) released supplemental analyses of urine samples collected for the earlier National Health and Nutrition Examination Survey (NHANES 2001-2002).[FN1: http://www.cdc.gov/nchs/about/major/nhanes/] That new data was based on an improved analysis for perchlorate that was sensitive to 0.05 ppb,[FN2: Valentin- Blasini L, et al.; Anal. Chem. 77: 2475-2481 (2005)] and showed that every one of the participants had measurable levels of perchlorate in their urine.

A statistical analysis of that data by Blount et al.[FN3: Blount BC, et al.; Environ Health Perspect. 114: 1865-71 (2006)] claimed a correlation between very small amounts of perchlorate and reduced thyroid T4 hormones in iodide deficient women. They suggested that extremely low levels of perchlorate could affect the health of such women. The Blount article has been cited as evidence that the MCL of 6 ppb issued by the California Department of Public Health is too high.

The urinary analyses reported by the CDC included more than just perchlorate. Some 2800 individual urine samples were analyzed by the CDC for perchlorate, thiocyanate, nitrate, and iodine. The results of those urine analyses were downloaded from the CDC, copied into a spreadsheet, and are analyzed here to a relatively simple extent. The frequency distribution of the perchlorate concentration is shown in Figure 1, and the cumulative distribution is shown in Figure 3. This population has a median urine perchlorate value of 4.0 ppb and a 10%-90% range of 1.2 - 10 ppb, surprisingly high values.

Figure 1. Distribution of Perchlorate Analysis [see PDF docket ID EPA-HQ- OW-2009-0297-0419]

Figure 3. Cumulative Distribution [see PDF docket ID EPA-HQ-OW-2009-0297-0419]

What is the source of this perchlorate? The biological half life of perchlorate in the body is only eight hours.[FN4: Greer MA, et al.; Environ Health Perspect 110: 927-937 (2002)] That means that every 8 hours, an individual excretes half the perchlorate from his body. Since perchlorate is not detected in about 96% of community water supplies, water cannot be the source of that urinary perchlorate. The detected perchlorate must be coming from dietary intake (vegetables, grains, milk, meat, medication, etc.). The perchlorate intake must be continual or it would soon drop to zero.

T4 HORMONE CORRELATION WITH URINARY PERCHLORATE

Blount's statistical analysis (fn.3) showing a perchlorate-T4 correlation was based on a regression of serum T4 concentrations vs. the logarithm of the urinary perchlorate concentration. (Log[ClO4-] is a normally distributed parameter in the population, while [ClO4-] is not.) The CDC data on urinary analyses yielded 416 female persons of age >=12 years and <100 ppb urinary iodide [the criterion for iodide deficiency] and where T4 data were also available. Blount's correlation cites a sample size of 348, an elimination of 16% of the samples. The referenced article discusses complicated procedures that were used for eliminating samples, but gives few details of those methods.

The results of this analysis here for 416 persons are summarized in the Table 4 below, with a comparison to Blount's numbers. The simple linear regression of the data without sample elimination and weighting shows some but much less correlation than Bount's. Figure 5 is a scatter plot for the perchlorate-T4 analysis using all the perchlorate data with no sample elimination. The line in this figure is calculated from the slope and intercept determined by the least squares fit to the 416 data points.

Figure 5. Correlation of Thyroid t4 with Perchlorate [see PDF docket ID EPA-HQ- OW-2009-0297-0419]

The correlation coefficients in Table 4 show a 10 fold better correlation by Blount than was achieved here. Blount declares his correlation to be statistically significant, but it apparently required extensive sample pruning to achieve those results. Our correlation here is weaker and would probably not be considered statistically significant. The CDC cautions against using their data without taking into account their study design and associated sample weights. When sample weights were incorporated into the frequency distribution, there was a small but not significant difference. With CDC sample weights, the median urinary perchlorate value was projected to be 3.8 ppb for the US population instead of 4.0 ppb for the sample population. However, the simple regression used in Table 4 and Figure 5 could not accommodate sample weights.

Did this analysis confirm Blount's correlation? These results are a limited confirmation of Blount's correlation, but not necessarily of his conclusions. The implied connection between perchlorate and T4 is tenuous at best.

Table 4. Statistical Analyses of CDC Data [see PDF docket ID EPA-HQ- OW-2009-0297-0419]

Attempts here using the released CDC data to demonstrate a similar effect by nitrate were unsuccessful. The results of simple linear regression of T4 levels against nitrate concentration and against log nitrate concentration are also summarized in Table 4 above.

In this analysis, there seems to be no connection between nitrate and T4. All the anion data are for urinary concentrations, whereas the iodide uptake occurs in the serum near the NIS. One might expect perchlorate, which is metabolically inert, to have similar concentrations in serum and urine. On the contrary, nitrate is not equally inert, and there could be sizable differences between serum nitrate and urinary nitrate. That might explain why no nitrate effect was seen.

The truly surprising result of the CDC data is the appearance of urinary perchlorate in every individual tested. Even more surprising is the 4 ppb median value. This can only be explained by food and not contaminated water. Considering the short half life of perchlorate in the body and for discussion assuming no source for it other than water, urinary concentrations are virtually equivalent to drinking water of the same concentration, namely more than 4 ppb for 50% of the population and more than 10 ppb for 10% of the population.

Response: EPA believes that perchlorate exposure may result from both food and drinking water. Previous analyses have estimated the portion of the perchlorate exposure from food. EPA considered the portion of perchlorate exposure from food in developing the potential alternative HRLs. See responses to comment IDs 20616 and 20886 under comment code 4000.
EPA believes that Blount's interpretation of the relationship between T4 and perchlorate concentrations as reported in the peer reviewed literature are authoritative. Blount lists the shortcomings of his analysis in his paper.
EPA does not believe that the widespread presence of perchlorate in food overrides the need for public health risk reduction for persons served by PWSs with perchlorate contamination. The Agency presented an extensive evaluation of dietary exposure to perchlorate in the October 2008 and August 2009 notices (73 FR 60262; USEPA 2008a and 74 FR 41883; USEPA 2009b). EPA recognizes that a drinking water regulation would not eliminate total perchlorate exposure, but believes that the reduction in perchlorate exposure in drinking water presents a meaningful opportunity for health risk reduction for persons served by PWSs contaminated by perchlorate.

Commenter Name: Richard M. Peekema
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0419
EPA Comment ID: 28686
EPA Comment Code: 4210

Comment: IMPORTANCE OF OTHER ANIONS

Other anions cannot be ignored in assessing the level of perchlorate that sensitive individual can tolerate. The following table summarizes the CDC data released on urinary concentration and the relative potency established for them. Tonacchera et al.[FN5: Tonacchera M, et al.; Thyroid 14:1012-1019 (2004)] have shown perchlorate to be 15, 30, and 240 times more potent than thiocyanate, iodide, and nitrate respectively, for inhibiting radioactive iodide uptake in the Human Sodium Iodide Symporter (NIS). The relative blocking potency values reported by Tonacchera are shown in Table 2.

Table 2. Anion Concentrations & NIS Potency [see PDF docket ID EPA-HQ- OW-2009-0297-0419]

In view of the urinary nitrate concentrations and the NIS potency shown in Table 2 above, one might expect to see a similar correlation between nitrate and the T4 hormone in iodide deficient women. Even though 240 times less potent than perchlorate, nitrate at 53,000 ppb would be equivalent to 221 ppb perchlorate which would have influenced T4. Attempts here using the released CDC data to demonstrate a similar effect by nitrate were unsuccessful. The results of simple linear regression of T4 levels against nitrate concentration and against log nitrate concentration were summarized earlier in Table 4.

Response: Nitrate shares a common mode of action with perchlorate. However, data do not exist at this time to permit a scientifically defensible estimation of the relative potency of perchlorate and nitrate. The Tonacchera paper, an *in vitro* study evaluating the function of human receptors hybridized into animal cells, does not provide sufficient evidence to support a meaningful comparison.

EPA Comment Code: 4220 Biomonitoring -- breast milk studies discussed in the notice

Individual Comments
Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20992
EPA Comment Code: 4220

Comment: Finally, other recent studies have demonstrated that perchlorate is actively transported into mammary epithelial cells by the sodium-iodide symporter (NIS), resulting in an accumulation of perchlorate in breast milk.[FN27: Dohan, O, C Portulano, C. Basquin, A Reyna-Noyra, LM Amzel, and N Carrasco. 2007. The Na+/I- symporter (NIS) mediates electroneutral active transport of the environmental pollutant perchlorate. PNAS 104(51):20250-20255.],[FN28: Dasgupta, P. K., Kirk, A. B., Dyke, J. V., and Ohira, S.-I. (2008). Intake of Iodine and Perchlorate and Excretion in Human Milk. Environ. Sci. Technol. 42, 8115-8121.] In fact, in the Dasgupta study, perchlorate was concentrated in breast milk three times more than iodine. Also of note, only one infant out of 13 in this study was found to have adequate iodine intake.

EPA has not adequately accounted for the concentrations of perchlorate in breast milk, the unique susceptibility of breast feeding neonates, or the fact that a significant portion of the U.S. population is iodine deficient, and therefore more susceptible to perchlorate toxicity.

Response: In the October 2008 notice EPA discusses a number of studies that investigated perchlorate in human breast milk including perchlorate concentrations. See response to comment code 2100 for a discussion of EPA's RfD and how that value both accounts for the most sensitive populations who are expose to perchlorate including iodine deficient populations. See response to comment code 5220 for a discussion of alternative HRLs. EPA has examined the relative sensitivity of the breast fed infant as part of its analysis for this regulatory determination as shown in Table 1 of the August 19 2009 Federal Register Notice.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21063
EPA Comment Code: 4220

Comment: i. Tellez et al. (2005)

This was a longitudinal epidemiologic study of the effects of environmental perchlorate exposure on the thyroidal status of pregnant women and neonates. Perchlorate is found naturally at high levels in Chilean soils and water supplies. Some have questioned the relevance of this study to the U.S. population as historically, Chile has had high levels of dietary iodide supplementations. However, this supplementation has been decreased to levels that are similar to U.S. levels. In this study, the maternal excretion (and therefore ingestion) of iodine was at levels that were between those reported in NHANES I and NHANES III. The authors measured maternal and neonatal TSH, Tg, and free

T4. They also measured neonatal birth weight, length, and head circumference. They found that "...perchlorate in drinking water at 114 ug/L did not cause changes in neonatal thyroid function or fetal growth retardation." The levels of iodine in breast milk were not associated with perchlorate exposure. The levels of maternal iodine in urine were intermediate to that found in NHANES I and NHANES III and consistent with the World Health Organization (WHO) recommendations. This study strengthens the evidence that the RfD and HRL are conservative health based values.

Response: The data underlying the definition of iodide uptake inhibition as a precursor effect and the relationship of iodide uptake inhibition to the continuum of adverse outcomes may not reflect the relationship of the precursor event to adverse outcomes in children. We know that thyroid hormone status in neonates and infants is less resilient than in adults. That is, in general, neonates and infants may not have iodide stores sufficient to offset the effects of reduced iodide uptake. The less resilient neonatal and infant system makes the exposure gap between a precursor event (iodide uptake inhibition due to perchlorate) and reduced T3/T4 levels likely to be narrower than for adults, and in fact, the distinction between the two may be blurred for the very young (Greer et al., 2002; Savin et al., 2003; van den Hove et al., 1999). The NAS noted that, "[T]he minimal prolonged decrease in thyroid hormone production that would be associated with adverse health effects is not known; any decrease is potentially more likely to have adverse effects in sensitive populations (people with thyroid disorders, pregnant women, fetuses, and infants) but data are not available to determine the magnitude of the decrease needed to cause adverse effects in those populations." See today's Federal Register notice for further discussion of EPA's determination that perchlorate may have an adverse impact on human health.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21064
EPA Comment Code: 4220

Comment: ii. Amitai et al. (2007)

This ecological study aimed to "...assess the effect of gestational perchlorate exposure through drinking water on neonatal thyroxine (T4)" by comparing T4 levels among newborns whose mothers lived in areas where drinking water perchlorate levels were very high (>=340 ug/L), high (42-94 ug/L), or low (<3 ug/L). T4 levels were measured within 36 to 48 hours after birth, but there was no comment on whether the infants were breast fed or formula fed during the postnatal period. They found that there were no differences between neonatal T4 levels among the groups. This study provides evidence that the current RfD and values greater are conservative and health protective to the most sensitive individuals in the population.

Response: Please see the response to comment ID 21063 under comment code 4220.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21076
EPA Comment Code: 4220

Comment: C. Breast Milk Studies

For many infants, breast milk is the sole source of food and therefore represents the greatest potential exposure to perchlorate. Although the population theoretically considered the most susceptible to the effects of high levels of perchlorate is developing fetuses, the effects of doses of perchlorate that are sufficiently high to block iodide uptake by the thyroid may alter normal growth and development in infants and children. Taken together, the following studies show that there is no association between environmentally relevant levels of perchlorate in drinking water and perchlorate or iodide in breast milk. Furthermore, no effect, adverse or otherwise, has been found due to environmentally relevant doses of perchlorate.

i. Pearce et al. (2007b)

The objective of the Pearce et al. study was "to determine whether breast milk iodine concentrations in Boston-area women are adequate for infant nutrition, and whether breast milk iodine concentrations may be associated with environmental perchlorate or cigarette smoke exposure." Pearce et al. measured breast milk iodine and perchlorate concentrations as well as iodine, perchlorate, and cotinine in urine. They then compared the levels found in breast milk to 17 commercial infant formulae. Neither breast milk perchlorate nor urinary perchlorate levels were significantly correlated with breast milk iodine concentrations. Although perchlorate was detectable in infant formulae, the levels were lower than that in breast milk. A significant number of women in this study had iodine levels that were insufficient to meet the infant's needs, but the authors did not suggest this was due to perchlorate exposure or that it represents a chronic iodine deficiency.

ii. Kirk et al. (2005)

With the aim to determine what amount of perchlorate children are exposed to, Kirk et al. measured perchlorate and iodide levels in cow and human breast milk and compared these numbers to corresponding levels of perchlorate in drinking water in the area. Perchlorate was measurable in 81 of the 82 samples. The average perchlorate levels in cow milk and human milk were 2 and 10.5 ug/L, respectively. The maximum values of cow and human milk were 11 and 92 ug/L, respectively. There was no correlation between levels of perchlorate in breast milk and perchlorate in drinking water. They speculated that there was a correlation between higher levels of perchlorate and lower levels of iodine in breast milk.[FN7: The Kirk et al study uses an arbitrary and non-scientific method of speculating on this relationship. Kirk et al., write: "...we divide iodide levels [in human breast milk] in two groups, those above 60 ug/L and those below, this being the iodide content for many infant feed formulas"; "we...divide perchlorate content in two groups, high and low, in this case arbitrarily dividing the span of the observed perchlorate range in two equal halves." and "at this point with limited resources, we have been able to analyze only a few samples. Thus, they divide data set using no scientific rationale and then exclude data. The authors state, "If we take all the available data, there is no meaningful correlation between the perchlorate and iodide levels in breast milk."] However, this relationship only existed for the breast milk samples with the highest perchlorate levels (6 subjects out of 82). The authors recognize that this relationship may be coincidental due to the small number of samples with perchlorate levels greater than 10 ug/L, stating that "If we take all the available data, there is no meaningful correlation between the perchlorate and iodide levels in breast milk." As with previous studies, due to the design, this study is not able to evaluate a causal relationship.

iii. Dasgupta et al. (2008)

In a very recently released study, Dasgupta et al. report the results of their study. "The objective of this present study was to study the excretion of perchlorate, thiocyanate, and iodine in milk and urine and relate the observed pattern within the broad framework of parallel / competitive transport by the NIS." Using breast milk and urine samples from 13 lactating women and using EPA default values for infant body weights and milk intakes, the authors mathematically modeled infant intakes and doses of iodide, perchlorate, and thiocyanate. They calculated the fraction of iodide, perchlorate, and thiocyanate in breast milk compared to the total that is excreted in both breast milk and urine. They used a ratio of these fractions in milk to determine the selectivity of either perchlorate or thiocyanate over iodide. They report "that 12 of 13 infants did not have an adequate intake of iodine...and 9 out of 13 infants were likely ingesting perchlorate at a level exceeding the reference dose..." They also concluded that the selectivity of perchlorate over iodide was 3.14 +/- 1.2.

[Text Box: Taken together, studies on perchlorate in breast milk show that there is no association between environmentally relevant levels of perchlorate in drinking water and perchlorate or iodide in breast milk. Furthermore, no effect, adverse or otherwise, has been found due to environmentally relevant doses of perchlorate.]

There are a number of concerns related to the experimental design of this paper. The population is small and there is no information on the selection process of the participants (e.g., they are not a random sample). There are only three biological variables that were measured from these women. The rest of the variables, including the variables used to derive the conclusions, are calculated from these these three in addition to using default values for infant intake and infant weights. The three measurements were the concentrations of of perchlorate, iodine, and thiocyanate in both urine and breast milk. Where other research has measured more biologically relevant information, such as serum concentrations of analytes which would be most reflective of relative concentrations at the NIS (Tonacchara et al., 2004; Pearce et al., 2007) thus, this work is limited. The estimated doses, the key variable for understanding possible NIS effects, are based on average body weight and intakes for an infant of that age with the concentration in breast milk. For such a simple and critical variable, it is suprising that actual body weights were not measured.

In addition to study design, the data presented in this paper appears to contradict the interpretation by the authors of the paper. Based on estimated weights, the authors state that 9 out of 13 infants are consuming daily doses in excess of the RfD. However, from examining Table 1 from Dasgupta et al., there are 8 infants who exceed the RfD of 0.7 ug/kg-d (subjects 1, 2, 8, 11, 13, 15, 16, 20). Furthermore, if one reviews these estimates to measured variables, the infants with estimated perchlorate doses greater than the RfD are also estimated to have the greatest iodine intake. By plotting the values for total iodide excretion (column 4), total perchlorate excretion (column 7), estimated maternal breast milk iodide excretion (equivalent to estimated infant iodide intake; column 5), and estimated maternal breast milk perchlorate excretion (product of total perchlorate excreted and percent of perchlorate in milk; column 7 x column 9) found in Table 1 of the paper, the results demonstrate that perchlorate and iodide are positively correlated (See Figure 3). If perchlorate was inhibiting the transport of iodide into milk, the association would be negative.

[Figure 2: Plotting of data reported by Dasgupta et al., 2008 to illustrate the association between concentrations of iodine and perchlorate in urine and milk in lactating women - See PDF Docket ID EPA-HQ-OW-2008-0692-1855]

In addition to the concerns regarding interpretation of the data presented in this paper, there are concerns about the interpretation of their previous work (Kirk et al., 2005) and how that study impacts this recent study. For example, Dasgupta et al. state in this current paper that "in real mothers perchlorate does inhibit the transport of iodine into milk and because of competitive inhibition both analytes cannot be high at the same time." However, this statement is based on a previous study in which the researchers defined their cut off values[FN8: The cutpoints from Kirk et al. (2005) were defined as follows: High iodide in breast milk was greater than 60 ug/L and high perchlorate in breast milk was greater than 20 ug/L.] above which milk iodide or perchlorate were considered "high." They report that no milk samples had both high perchlorate and high iodide (Kirk et al., 2005). In the present study, they report the same trend although they do not define a cut off value. However, if the previous cut off values are applied to the current study, there are many samples that had simultaneously high perchlorate and iodide (Figure 3). Based on the previous conclusions about competitive inhibition of analytes (Kirk et al., 2005), this study does not demonstrate that perchlorate competitively inhibits iodide transport into milk at the concentrations experienced by these women.

Response: In the October 2008 notice EPA discusses a number of studies that investigated perchlorate concentrations in human breast milk. Poor iodide uptake and subsequent impairment of the thyroid function in pregnant and lactating women have been linked to delayed development and decreased learning capability in their infants and children (NRC, 2005). Additionally, deficiency during childhood reduces child growth and cognitive motor function (Zimmerman, 2009). EPA has considered the portions of the population who are most sensitive to the effects of perchlorate and has determined that perchlorate may have an adverse effect on the health of persons.

Please also see the response to comment ID 20992 under comment code 4220.

EPA Comment Code: 4230 Biomonitoring -- other biomonitoring studies, models, and data for EPA to consider (other than NHANES and breast milk studies discussed in the notice)

Individual Comments
Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21077
EPA Comment Code: 4230

Comment: iv. Dohan et al. (2007)

Animal, particularly rodent, studies are an implicit and valuable aspect of toxicology. There are, however, significant differences between human and rodent thyroid physiology. U.S. EPA states, "The fundamental mechanisms involved in the function and regulation of the pituitary-hypothalamus-thyroid system in rats are qualitatively similar to those in humans. However, differences in binding proteins, binding affinities of the proteins for the hormones, turnover rates of hormones, and thyroid stimulation by placental hormones lead to important quantitative differences between the two species. The biochemical and physiologic differences between rats and humans related to the thyroid affect their responses to goitrogens, such as perchlorate. Therefore, although studies in rats provide useful qualitative information on potential adverse effects of perchlorate exposure, they are limited in their utility for quantitatively assessing human health risk associated with perchlorate exposure" (U.S. EPA, 2005).

The main purpose of the Dohan et al. publication is to demonstrate that perchlorate crosses cell membranes via the NIS; to demonstrate perchlorate's ability to be excreted in breast milk; and to develop a mathematical model to characterize their experimental results. The in vitro experiment and system they use is unique, creative, and provides the first evidence of perchlorate crossing a cell membrane using Mardin-Darby canine kidney (MDCK) cells transfected with the human NIS. It provides further evidence regarding questions about breast milk perchlorate levels and whether perchlorate blocks iodide at the symporter or competes against iodide in crossing the NIS. Thus, it decreases uncertainty in the risk assessment process. It is important to remember that this is the first study of its kind, it was conducted in vitro (cell culture), and it was conducted in a non-human cell line with artificially introduced human symporters. From a perspective on cell membrane transport, this work provides qualitative information.

The author's discussion of the in vivo part of the study's relevance to environmental exposures of perchlorate and human health is, however, far reaching and not supported by the results of this experiment. High acute doses of perchlorate were given to the rats. The rats were given an intraperitoneal injection of nearly 8 mg/kg/d in addition to a drinking water exposure of 13.6 mg/kg/d.[FN9: Assumes a 250 g rat with a daily water intake of 5.5 ml/100 g body weight.] The perchlorate doses administered in this study are high enough such that they should effectively block, with complete inhibition, iodide transport by the NIS in these rats, which provides no information about the effects at environmentally relevant doses. The results cannot be used to draw conclusions about what happens from a human health standpoint or mechanistic function at environmentally relevant concentrations.

Response: In the October 2008 notice EPA discusses a number of studies that investigated perchlorate concentrations in human breast milk. In today's notice EPA discusses the uncertainty about the point in the continuum of effects at which adversity occurs, and that these were major considerations in determining whether perchlorate is likely to have an adverse effect on health at a range of life stages. The conclusions of the study by Dohan et al. (2007) that NIS translocates perchlorate in epithelial mammary cells in vivo, based on rat models, represents a valuable contribution to the current scientific literature on the biological mechanisms of perchlorate uptake in mammary cells and its potential inhibitory effect on iodine, and its potential relevance to nursing neonates and infants.

The data underlying the definition of iodide uptake inhibition as a precursor effect and the relationship of iodide uptake inhibition to the continuum of adverse outcomes reflects an understanding of effects in adults; it may not reflect the relationship of the precursor event to adverse outcomes in neonates and infants, who may not have iodide stores sufficient to offset the effects of reduced iodide uptake. The less resilient neonatal and infant system makes the exposure gap between a precursor event (iodide uptake inhibition due to perchlorate) and reduced T3/T4 levels likely to be narrower than for adults, and in fact, the distinction between the two may be blurred for the very young (Greer et al., 2002; Savin et al., 2003; van den Hove et al., 1999). The NRC noted that, "[T]he minimal prolonged decrease in thyroid hormone production that would be associated with adverse health effects is not known; any decrease is potentially more likely to have adverse effects in sensitive populations (people with thyroid disorders, pregnant women, fetuses, and infants) but data are not available to determine the magnitude of the decrease needed to cause adverse effects in those populations."

EPA Comment Code: 4300 Other perchlorate exposure studies, models, and data for EPA to consider (other than drinking water, diet, and biomonitoring)

Individual Comments
Commenter Name: Erik Lokensgard
Commenter Organization: Division of the Biological Sciences, University of Chicago
EPA Document ID: EPA-HQ-OW-2008-0692-0320
EPA Comment ID: 19808
EPA Comment Code: 4300

Comment: I also recommend that pool chlorination systems be investigated for their potential role in perchlorate pollution. I'm sure that every family would prefer safe tap water to every family having a pool.

Thank you for your time, Erik Lokensgard Division of the Biological Sciences University of Chicago

Response: There may be perchlorate generated from stored hypochlorite solutions used in pools; however, under this action EPA is evaluating whether perchlorate should be regulated under the Safe Drinking Water Act. EPA is not seeking to determine the source of perchlorate as part of this action.

Commenter Name: Jeremy Ginoza
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0635
EPA Comment ID: 19983
EPA Comment Code: 4300

Comment: Perchlorate has been shown in animal studies to disrupt thyroid function (see references below). Please err on the side of less public health exposure, not more. Place the burden not on the delicate balance of human organs and tissues, but on profitable corporations to act responsibly.

--Jeremy Ginoza, 4th year medical student

Effects of maternal exposure to ammonium perchlorate on thyroid function and the expression of thyroid-responsive genes in Japanese quail embryos. Chen Y, Sible JC, McNabb FM. Gen Comp Endocrinol. 2008 Sep 6.

"Our study shows that maternal perchlorate exposure led to embryonic hypothyroidism and may have interfered with embryonic development."

"Embryos from eggs of perchlorate-exposed hens had hypertrophied thyroid glands and significantly lower thyroidal hormone storage, indicating hypothyroidism in these embryos. The embryonic hypothyroidism was associated with decreased embryonic growth, delayed hatching and greater mortality during hatching."

Effects of prolonged exposure to perchlorate on thyroid and reproductive function in zebrafish. Mukhi S, PatiÃ±o R. Toxicol Sci. 2007 Apr;96(2):246-54. Epub 2007 Jan 6.

"At 10 weeks of exposure, perchlorate at both concentrations caused thyroidal hypertrophy and colloid depletion."

"In conclusion, prolonged exposure of adult zebrafish to perchlorate not only disrupts their thyroid endocrine system but also impairs reproduction and influences early F1 development."

Response: EPA has decided to regulate perchlorate in drinking water. See response to comment code 6120.

EPA Comment Code: 5000 SDWA Criteria

Individual Comments
Commenter Name: Thomas L. Schoaf
Commenter Organization: Cities of Litchfield Park and Goodyear, AZ
EPA Document ID: EPA-HQ-OW-2008-0692-1552
EPA Comment ID: 20519
EPA Comment Code: 5000

Comment: Under the Safe Drinking Water Act (SDWA), the EPA considers three criteria to determine if a drinking water standard should be established for a contaminant. Those criteria are that: i) there is a potential adverse human health effect ; ii) it is known or likely to occur at a level and frequency of concern in Public Water Systems (PWSs); and, iii) regulation presents a meaningful opportunity for health risk reduction.

The EPA has determined that perchlorate presents an adverse human health effect. It is important to note that the EPA has also determined that perchlorate has a greater impact on sensitive populations, specifically pregnant women and developing fetuses.

In evaluating potential exposure, the EPA concluded that perchlorate occurs at levels in excess of its selected health risk level threshold of 15 ug/L in less than 1% of PWSs. Even at this percentage, the EPA reports that its upper end estimate of population exposed to perchlorate at levels in excess of its selected health risk level is 2 million people. If the EPA had applied a more conservative relative source contribution factor, the upper end exposure estimate could be as high as 14 million people. We think that these exposure estimates alone warrant a determination that "regulation presents a meaningful opportunity for risk reduction." However, we are concerned that the EPA's evaluation of impacted public water supply systems (PWSs) may underestimate potential future exposure. By focusing only on known contamination at existing PWSs, the EPA does not consider likely impacts- one of the SDWA criteria. For example, without the strength of a promulgated standard to require cleanup of the impacted aquifers at the PGA North Superfund Site, exposure to perchlorate will likely occur as future PWSs or future entry points to existing PWSs are brought on-line. By considering likely occurrences of perchlorate exposure, we believe that there is a known or likely exposure at a level and frequency of concern.

Response: EPA has determined that regulation of perchlorate in drinking water systems presents a meaningful opportunity to reduce health risk for persons served by public water systems. See response to comment code 6120.

Commenter Name: Ron Curry
Commenter Organization: New Mexico Environment Department
EPA Document ID: EPA-HQ-OW-2008-0692-1796
EPA Comment ID: 20935
EPA Comment Code: 5000

Comment: Section 1412(b)(1)(A) of the SDWA provides that the EPA Administrator shall "promulgate a national primary drinking water regulation for a contaminant if the Administrator determines that:

(i) the contaminant may have an adverse effect on the health of persons; (ii)the contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and (iii)in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

42 U.S.C. [section] 300g-1(b)(1)(A) (Westlaw 2008).

Section 1412(b)(1)(C) of the SDWA further provides that in determining whether to regulate drinking water contaminants, the Administrator must take into consideration:

the effect of such contaminants upon subgroups that comprise a meaningful portion of the general population (such as infants, children, pregnant women, the elderly, individuals with a history of serious illness, or other subpopulations) that are identifiable as being at greater risk of adverse health effects due to exposure to contaminants in drinking water than the general population.

42 U.S.C. [section] 300g-1(b)(1)(C) (Westlaw 2008).

The Environment Department respectfully submits that each of the three criteria in section 1412(b)(1)(A) is met for perchlorate. Moreover, the risk of adverse health effects from perchlorate ingestion is greater for certain sensitive subgroups of the general population as described in section 1412(b)(1)(C).

Response: See response to comment code 6120.

Commenter Name: Ron Curry
Commenter Organization: New Mexico Environment Department
EPA Document ID: EPA-HQ-OW-2008-0692-1796
EPA Comment ID: 20939
EPA Comment Code: 5000

Comment: For EPA to base a final decision not to establish primary drinking water regulations for perchlorate under the SDWA on this analysis would be arbitrary, capricious, and not in accordance with the plain requirements of the SDWA.

Response: See response to comment code 6120.

Commenter Name: Caroline Baier-Anderson, PhD
Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20942
EPA Comment Code: 5000

Comment: Perchlorate Meets the Three Criteria Needed to Justify Promulgation of a National Standard There are three criteria that must be met to justify the promulgation of a national public drinking water regulation:

a) The contaminant may have an adverse effect on human health b) The contaminant occurs with a frequency and at levels of public health concern, and c) The promulgation of standards presents a meaningful opportunity to reduce health risk.

In our view, perchlorate meets all three of these criteria: perchlorate poses a significant health risk, is present at sufficient levels and in a sufficient number of public water systems to constitute a public health concern, and by promulgating a standard, EPA has a meaningful opportunity to reduce health risk.

Response: See response to comment code 6120.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21093
EPA Comment Code: 5000

Comment: III. The Current Scientific Literature Provides Overwhelming Support for EPA's Findings under the Safe Drinking Water Act's Criteria for this Determination

In the SDWA, EPA is directed by Congress to make a determination whether to set a National Primary Drinking Water Regulation (NPDWR) based on the following criteria:

a) the contaminant may have an adverse effect on the health of persons;

b) the contaminant is known to occur in public water systems with a frequency and at levels of public health concern; and,

c) in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems (73 FR 60264).

Response: See response to comment code 6120.

Commenter Name: Anthony Russo
Commenter Organization: Chemistry Council of New Jersey (CCNJ)
EPA Document ID: EPA-HQ-OW-2009-0297-0673
EPA Comment ID: 28689
EPA Comment Code: 5000

Comment: The Agency must be able to support its determination with credible, properly interpreted science. Pursuant to the SDWA, EPA's final regulatory determination whether to establish a primary drinking water standard for perchlorate is based upon the following statutory criteria:

* The contaminant may have an adverse effect on the health of persons; * The contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and * In the sole judgment of the

Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

Response: No response necessary for this comment.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28825
EPA Comment Code: 5000

Comment: September 17, 2009

Water Docket Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Ave., NW Washington, DC 20460

Re: Comments on the Drinking Water: Perchlorate Supplemental Request for Comments Docket ID No. EPA-HQ-OW-2009-0297

The Association of Metropolitan Water Agencies (AMWA) appreciates the opportunity to comment on the preliminary regulatory determination for perchlorate as listed in the August 19, 2009 Federal Register (74 FR 41883). AMWA strongly supports the process required by the 1996 Amendments to the Safe Drinking Water Act that places a strong emphasis on science and focuses on contaminants which: may have an adverse effect on humans; occur or are likely to occur at levels of public health concern; and provide a meaningful opportunity for health risk reduction.

Response: No response necessary for this comment.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28871
EPA Comment Code: 5000

Comment: 4. Science-based considerations: The Safe Drinking Water Act (SDWA) has three requirements-all three of which must be met to satisfy the law. The scientific literature addresses these requirements for perchlorate. The science clearly shows EPA's statutory criteria for setting a standard are unmet in this case:

Response: EPA disagrees with the statement that "the science clearly shows EPA's statutory criteria for setting a standard are unmet." In making final regulatory determinations, EPA uses the criteria mandated by the 1996 SDWA Amendments. Specifically, EPA has found that perchlorate may have an adverse effect on the health of persons, that perchlorate occurs or there is a substantial likelihood that perchlorate will occur in public water systems with a frequency and at levels of public health concern, and that regulation of perchlorate in drinking water systems presents a meaningful opportunity for health risk reduction for persons served by public water systems. The Federal Register notice for this action describes how EPA evaluated these three criteria in light of the best available peer reviewed data to make a preliminary regulatory determination for perchlorate.

EPA Comment Code: 5100 SDWA Criterion #1 – EPA's determination that perchlorate may have adverse effects on the health of persons

Individual Comments
Commenter Name: Melanie A. Marty, Ph.D.
Commenter Organization: Children's Health Protection Advisory Committee
EPA Document ID: EPA-HQ-OW-2008-0692-0962
EPA Comment ID: 20421
EPA Comment Code: 5100

Comment: The Safe Drinking Water Act (SDWA) requires the Administrator to establish an MCL when three conditions are met. The CHPAC feels strongly that all three conditions are met in the case of perchlorate. The first condition, that the contaminant has an adverse effect on the health of persons, is met for perchlorate. Perchlorate interferes with thyroid function and can lower circulating thyroid hormone levels in humans; lowered thyroid hormone levels and consequent impacts on the developing brain have been demonstrated in perchlorate-dosed animals. The developing fetus and infants are vulnerable to perchlorate due to the exquisite sensitivity of brain development to thyroid hormone levels, and the fact that newborns have no stores of this hormone.

Response: See response to comment code 6120.

Commenter Name: Ron Curry
Commenter Organization: New Mexico Environment Department
EPA Document ID: EPA-HQ-OW-2008-0692-1796
EPA Comment ID: 20936
EPA Comment Code: 5100

Comment: As to the first criterion, it is without dispute that perchlorate in drinking water has anadverse effect on the health of persons. According to the National Research Council, perchlorate can adversely affect the function of the thyroid "because it is an ion that competitively inhibits the transport of iodide into the thyroid" by a protein known as the sodium/iodide symporter.[FN13: NATIONAL RESEARCH COUNCIL, HEALTH IMPLICATIONS OF PERCHLORATE INGESTION 6 (2005).] Iodide deficiency resulting from perchlorate ingestion is more likely to have a negative effect in sensitive populations, such as people with thyroid disorders, pregnant women, fetuses, and infants.[FN14: Id.] In pregnant women, severe iodide deficiency can result in major neurodevelopmental deficits and goiter in their offspring.[FN15: Id.] Lesser degrees of iodide deficiency may also cause important neurodevelopmental deficits in infants and children.[FN16: Id.] EPA expressly recognizes the adverse health effects of perchlorate ingestion.[FN17: See 73 Fed. Reg. 60262, 60275 (Oct. 10, 2008).]

Response: EPA agrees with the commenter. EPA believes the health risk is particularly high for infants and children with high drinking water consumption relative to their body weight.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0415
EPA Comment ID: 28846

EPA Comment Code: 5100

Comment: The study by Mendez et.al. [FN13: Mendez, W., Dederick' E., and J. Cohen. 2009. Drinking water contribution to aggregate perchlorate intake of reproductive-age women in the United States estimated by dietary intake simulation and analysis of urinary excretion data. Journal of Exposure Science and Environmental Epidemiology advance online publication 16 September 2009.] further supports findings that the NOEL based RfD is sufficiently conservative and health protective of sensitive subpopulations. This study finds that the total dietary exposure (food and drinking water) of reproductive age women in the U.S. is approximately one-third of the RfD for perchlorate at the 95th percentile, which is complementary to the findings of the joint assessment prepared by EPA-CDC. Given this evidence related to limited exposure potentials and estimated intakes well below the RfD, it is clear that there is limited potential for perchlorate to present a significant adverse affect on the nation's health, including sensitive subpopulations.

Response:

EPA disagrees that there is a limited potential for perchlorate to present a significant adverse effect on the nation's health, including sensitive subpopulations. EPA has determined that perchlorate occurs or there is a substantial likelihood that perchlorate will occur with a frequency and at levels of health concern in public water systems. EPA has made this determination by comparing the best available data on the occurrence of perchlorate in PWSs to potential health reference levels (HRLs) for perchlorate.

Since the NRC also identified infants and developing children as additional life stages, EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 μg/L to 47 μg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These HRLs are calculated based on individuals who consume an average amount of perchlorate from food (except for pregnant women where EPA used a 90th percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts.

EPA is evaluating these potential alternative HRLs and considers them to be levels of public health concern for purposes of this determination.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28872
EPA Comment Code: 5100

Comment: a) The SDWA requires that the contaminant must have an adverse effect on the health of persons. The weight-of-evidence, after examining the published scientific literature, demonstrates no documented adverse effects in humans exposed to perchlorate at environmental levels.

Response:

EPA disagrees. EPA disagrees that the "weight of evidence" demonstrates no documented adverse effects in humans exposed to perchlorate at environmental levels. See today's final regulatory

determination for further discussion of the basis of EPA's conclusion that perchlorate may have an adverse health effect on persons.

EPA has determined that perchlorate meets SDWA's criteria for regulating a contaminant —that is, perchlorate may have an adverse effect on the health of persons; perchlorate is known to occur or there is a substantial likelihood that perchlorate will occur in public water systems with a frequency and at levels of public health concern; and in the sole judgment of the Administrator, regulation of perchlorate in drinking water systems presents a meaningful opportunity for health risk reduction for persons served by public water systems.

After careful review and consideration of public comments on the May 2007, October 2008, and August 2009 notices, and information available at this time, EPA has made this determination by comparing the best available data on the occurrence of perchlorate in PWSs to potential health reference levels (HRLs) for perchlorate as discussed in the regulatory determination final notice.

Since the NRC also identified infants and developing children as additional life stages, EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 μg/L to 47 μg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These HRLs are calculated based on individuals who consume an average amount of perchlorate from food (except for pregnant women where EPA used a 90^{th} percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts.

EPA is evaluating these potential alternative HRLs and considers them to be levels of public health concern for purposes of this determination.

EPA Comment Code: 5200 SDWA Criterion #2 – EPA's determination that perchlorate occurs infrequently at levels of health concern in public water systems

Response to Code 5200:
EPA has determined that perchlorate occurs or there is a substantial likelihood that perchlorate will occur with a frequency and at levels of health concern in public water systems. EPA has made this determination by comparing the best available data on the occurrence of perchlorate in PWSs to potential health reference levels (HRLs) for perchlorate. EPA collected and analyzed drinking water occurrence data for perchlorate from 3,865 PWSs between 2001 and 2005 under the UCMR 1. The minimum reporting level (MRL) for perchlorate under the UCMR 1 was 4 μg/L. EPA found that 160 (approximately 4.1 percent) of the 3,865 PWSs that sampled and reported had at least 1 analytical detection of perchlorate (in at least 1 sampling point) at levels greater than or equal to the MRL of 4 μg/L. These 160 PWSs are located in 26 States and 2 territories. Of these 160 PWSs, 8 are systems serving 10,000 or fewer people and 152 are systems serving more than 10,000 people. These 160 systems reported 637 detections of perchlorate at levels greater than or equal to 4 μg/L, which is approximately 11.3 percent of the 5,629 samples collected by these 160 PWSs and approximately 1.9 percent of the 34,331 samples collected by all 3,865 PWSs. The average concentration of perchlorate for those samples with positive detections for perchlorate was 9.85 μg/L and the median concentration was 6.40 μg/L.

EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 μg/L to 47 μg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage.

Based on percent of public water system estimates for perchlorate above thresholds of interest in Table 1 in the Federal Register Notice, and the range of potential alternative HRLs, EPA has determined that perchlorate is known to occur or there is a substantial likelihood that it will occur with a frequency and at levels of public health concern.

In light of the discussion in this notice and the information available at this time, the Administrator finds that regulation of perchlorate in drinking water systems presents a meaningful opportunity for health risk reduction for persons served by public water systems. Therefore, EPA will initiate the process of proposing a NPDWR for perchlorate.

Individual Comments
Commenter Name: James Taft
Commenter Organization: Association of State Drinking Water Administrators (ASDWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0169
EPA Comment ID: 20286
EPA Comment Code: 5200

Comment: Perchlorate:

Based on state input, it does not appear that perchlorate is being detected in very many public water systems. Thus, while it may be a critical issue at a small number of water systems, it does not appear, at this stage, to be a nationwide problem that impacts most or all states.

Response: See response to comment code 5200.

Commenter Name: Melanie A. Marty, Ph.D.
Commenter Organization: Children's Health Protection Advisory Committee
EPA Document ID: EPA-HQ-OW-2008-0692-0962
EPA Comment ID: 20422
EPA Comment Code: 5200

Comment: The second condition, that the contaminant occurs in public water supplies with a frequency and level of public health concern, is also met for perchlorate. The UCMR data show that millions of Americans are exposed to perchlorate in public supplies at concentrations greater than 6 ug/L, the highest of three recently set state drinking water targets for perchlorate. The only way the second condition is not met is if an inappropriately high health benchmark is set. The CHPAC strongly feels that this is the case with USEPA's HRL of 15 ug/L as this would cause large numbers of infants to receive daily doses of perchlorate that are well above the Agency's RfD.

Response: See response to comment code 5200.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection
EPA Document ID: EPA-HQ-OW-2008-0692-1422
EPA Comment ID: 20435
EPA Comment Code: 5200

Comment: 10. EPA Underestimates Numbers of At Risk Citizens. Due to the fact that MassDEP believes the HRL should be 2 ppb we conclude more than 16.6 million people are exposed to unsafe levels of perchlorate in their drinking water, and that this is a significant national public health issue.

Response: Regarding your comment that EPA underestimated the number of people at risk, see response to comment code 5200. Regarding your comment that this is a significant national public health issue, EPA has determined that regulation of perchlorate in drinking water systems presents a meaningful opportunity to reduce health risk for persons served by public water systems. This action initiates the process to establish a national primary drinking water regulation for perchlorate including the maximum concentration of perchlorate that is allowed in public drinking water systems.

Commenter Name: Michael Dourson
Commenter Organization: Toxicology Excellence for Risk Assessment
EPA Document ID: EPA-HQ-OW-2008-0692-1562
EPA Comment ID: 20638
EPA Comment Code: 5200

Comment: Dear Sirs,

Based on EPA's analysis of exposure data and relative source contribution, we agree that perchlorate is not occurring in the public water supply at levels that cause concern for health risks.

Response: EPA disagrees with the commenter that the perchlorate is not occurring in the public water supply at levels that cause concern for health risks. See response to comment code 5200.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20907
EPA Comment Code: 5200

Comment: * Even EPA's own flawed assessment finds that up to 2 million people may be exposed to perchlorate at levels that are of concern and yet, EPA chooses not to take any meaningful action.

Response: EPA has determined that regulation of perchlorate in drinking water systems presents a meaningful opportunity to reduce health risk for persons served by public water systems. See response to comment code 6120.

Commenter Name: Ron Curry
Commenter Organization: New Mexico Environment Department
EPA Document ID: EPA-HQ-OW-2008-0692-1796
EPA Comment ID: 20937
EPA Comment Code: 5200

Comment: As to the second criterion, EPA estimates that 16,000 to 28,000 pregnant women would be exposed to perchlorate at levels exceeding the health reference level (HRL) of 15 "at any given time."[FN18: Id. at 60277.] EPA thus concludes that "perchlorate occurs infrequently at levels of health concern in public water systems."[FN19: Id.] EPA's analysis is seriously flawed for several reasons.

First, the analysis fails to consider future health effects on women who have not yet become pregnant, and on their future fetuses. This failure is at odds with the plain language ofthe SDWA. Section 1412(b)(1)(A)(ii) requires EPA to consider not only whether a contaminant is known presently to occur in public water systems so as to cause public health concern, but also whether "there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern."[FN20: 42 U.S.C. [section] 300g-1(b)(1)(A)(ii) (Westlaw 2008) (emphasis added).] Thus, Congress wisely directed EPA to consider potential future health effects in its analysis. But EPA has subtly avoided this consideration in its perchlorate analysis. EPA asks, "Is perchlorate known to occur or is there a substantial likelihood that perchlorate occurs at a frequency and at a level of public health concern in public water systems?"[FN21: 73 Fed. Reg. at 60275 (emphasis added).] EPA then answers this question in the negative because the agency finds that no more than 16,000 to 28,000 pregnant women "could be exposed at levels exceeding the HRL at any given time." EPA effectively takes a snapshot of perchlorate exposure at one instant in time. EPA does not take into account the millions of women who will become pregnant and who could be exposed to perchlorate above the HRL in future months, years, and decades. EPA's failure to account for future health effects is contrary to the SDWA.

Second, the analysis fails to consider health effects on infants. According to the National Research Council, infants comprise a subpopulation that is particularly sensitive to perchlorate exposure. For example, studies have shown that children with a mild iodide deficiency - which perchlorate can cause - have learning disabilities and perform less well on tests of mental and psychomotor ability.[FN22: NATIONAL RESEARCH COUNCIL, supra note 13, at 59.] Moreover, the HRL for infants is likely below the 15 ug/L that EPA determined for pregnant women.[FN23: See letter from Melanie A. Marty, Ph.D., Chair, Children's Health Protection Advisory Committee, to EPA Administrator Stephen L. Johnson, at 2 (Nov. 3, 2008).] EPA's failure to consider the adverse health effects of perchlorate ingestion on infants, a sensitive subgroup, in (preliminarily) determining that perchlorate occurs infrequently in public water systems at levels of health concern is also contrary to the SDWA.

Third, the analysis fails to take into consideration health effects on persons with thyroid disorders. According to the National Research Council, people with thyroid disorders would be expected to be more sensitive to the effects of perchlorate ingestion.[FN24: NATIONAL RESEARCH COUNCIL, supra note 13, at 51.] Again, EPA's failure to consider the adverse health effects of perchlorate ingestion on persons with thyroid disorders in (preliminarily) determining that perchlorate occurs only infrequently in public water systems at levels of public health concern is contrary to the SDWA.

Response: See response to comment code 5200. NRC specifies the fetus of a mother with hypothyroidism or iodine deficiency and low birthweight and premature infants as the most sensitive populations. Since the NRC also identified infants and developing children as additional life stages, EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 μg/L to 47 μg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These HRLs are calculated based on individuals who consume an average amount of perchlorate from food (except for pregnant women where EPA used a 90th percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts. EPA is evaluating these potential alternative HRLs and considers them to be levels of public health concern for purposes of this determination.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-2082
EPA Comment ID: 21028
EPA Comment Code: 5200

Comment: 11. Your letter asserts that millions are exposed to perchlorate at levels exceeding the 6 μg/L, the highest of the state MCLs to be established.

In our comments, the PSG has compared the risk opportunity from detects in public water systems (PWSs) between perchlorate and other compounds that EPA has decided not to regulate. The percentage of PWSs with perchlorate detections was very low (3.6 percent) compared to the next lowest unregulated compound, manganese at 68 percent. Sodium, for example, was detected in all PWSs. Perchlorate also has one of the lowest populations served by PWSs with detections above

half the HRL with 2.2 million people. Perchlorate is well within the range of values for the evaluation criterion EPA uses.

Additionally, it bears repeating that EPA has incorporated an additional level of conservatism into an already conservative and health protective NAS-based RfD. Specifically, any exposures above the RfD, if they indeed occur, must first be considered in the context of a non-adverse effect.

Response: Regarding the suggestion to compare the risk opportunity from detects in public water systems between perchlorate and other compounds that EPA has decided not to regulate, EPA does not believe it's appropriate to factor these comparisons into the decision whether to regulate a contaminant. The Administrator will make these determinations on a case-by-case, contaminant specific basis. In making a regulatory determination, the Administrator considers the adverse health effect of the particular contaminant at issue as well as the occurrence or likelihood of occurrence of the contaminant in public water systems with a frequency and at levels of public health concern. In addition, even if such a comparison were appropriate, perchlorate has, at least at the lower levels of public health concern identified, an occurrence that is substantially larger than most of the contaminants for which EPA has made a negative determination. Finally, it is the sole judgment of EPA's Administrator to determine whether there is a meaningful opportunity to reduce health risk for persons served by public water systems.
Regarding the comment that any exposures above the RfD must first be considered in the context of a non-adverse effect, the data underlying the definition of iodide uptake inhibition as a precursor effect and its relationship to the continuum of adverse thyroid outcomes reflects an understanding of effects in adults. The relationship of the precursor event to the adverse outcome in children has not been studied. Thyroid hormone status in neonates and infants is much less resilient than in adults. Generally speaking, they do not have iodide stores sufficient to offset the effects of reduced iodide uptake. Half-lives for circulating hormones are shorter than for adults, making infants and neonates less able to maintain stable hormone levels in the face of a chemical insult. The less resilient infant and neonatal system makes the exposure gap between a precursor event (iodide uptake inhibition due to perchlorate) and an adverse effect (reduced T3/T4 levels) much narrower than for adults. The distinction between the two may be blurred for the very young.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21096
EPA Comment Code: 5200

Comment: EPA's UCMR monitoring found a mean concentration of less than 10 ppb in systems with perchlorate - over 100 times lower than the NAS adverse effect level. Only a few systems have found any samples with concentrations greater than 100 ppb. Even the maximum level detected in the US is approximately 50 times lower than the dose at which the NAS panel determined adverse effects could begin. Specifically, the NAS panel noted that "...a sustained exposure of more than 0.4 mg/kg per day would most likely be required to cause a sufficient decline in iodide uptake and thyroid hormone production to result in adverse health effects in normal adults." (NAS 2005) For these reasons, perchlorate is not known or likely to occur in public water systems with a frequency and at levels of public health concern.

Response: See response to comment code 5200.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28873
EPA Comment Code: 5200

Comment: b) The SDWA requires that the contaminant must be known to occur in PWSs with a frequency and at levels of public health concern. Where perchlorate is found, it is at levels often an order of magnitude below levels that cause IUI, itself a nonadverse effect. EPA data indicate average perchlorate concentrations in public drinking water systems are <10 parts per billion (ppb), and 99% of samples were <7 ppb. These levels are all below the equivalent concentration corresponding to the RfD, assuming a standard EPA default body weight and drinking water consumption rate, as well as the HRL of 15 ppb proposed by EPA in 2008 (U.S. EPA, 2008a).

Response: See response to comment code 5200.

EPA Comment Code: 5210 Derivation of the RSC

Response to Code 5210: EPA routinely applies a relative source contribution (RSC) to allow for the possibility that not all exposure will come from water, recognizing the importance of keeping the total exposure dose (e.g., water plus diet) below the RfD.

EPA believes that use of an RSC for perchlorate is appropriate because the Greer et al. (2002) study, upon which the RfD is based, did not measure the levels of perchlorate in their food, and the sample size is small (37 healthy adults).

The RSC is based on the best available peer reviewed science from the FDA (Total Diet Study) and estimates of exposure based on the NHANES/UCMR data which are robust evaluations of dietary exposure to perchlorate. A more detailed discussion of the derivation of the RSC can be found in the 2009 Federal Register Notice.

Individual Comments
Commenter Name: Thomas Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0162
EPA Comment ID: 20268
EPA Comment Code: 5210

Comment: In developing a drinking water regulation for perchlorate, EPA needs to address the Relative Source Contribution (RSC) for perchlorate in food and water. The proposal in the May 1st Federal Register notice is a starting point for making an appropriate RSC decision. AWWA recommends that EPA not adjust for RSC, since the subjects in the Greer study were exposed to background levels of perchlorate in addition to an experimental dose, as discussed on pg. 24046 of the May 1st Federal Register notice.

Alternatively, if EPA doesn't accept the above recommendation, then EPA should derive the value of average daily rate of intake from background sources (ADRIB) from the mean (preferred approach) or upper tail (less preferred approach) of the NHANES data specific either to the entire sampled population or to individuals using bottled water. This background value should then be subtracted from the Reference Dose (RfD) and that result used to calculate the Drinking Water Equivalent Level (DWEL). This Modified ADRI approach better approximates the target average daily rate of intake (ADRI) that must be reached to ensure the RfD is not exceeded when water is added to the perchlorate contribution from all other sources combined (ADRIT).

From a technical perspective, some of the options presentation in the May 1st Federal Register simply do not make sense. For example, the EPA option of a regression of the NHANES urinary data versus UCMR is not feasible and should not be considered. It would result in only a couple of dozen data points, an insufficient number to allow a meaningful regression.

Appendix A [See Appendix A in PDF of docket ID EPA-HQ-OW-2007-0068-0162] to these comments is a report by Dr. Douglas Crawford- Brown of the University of North Carolina-Chapel Hill that was prepared on behalf of AWWA. Dr. Crawford- Brown's report explains the above

recommendations in greater detail, comparing and contrasting alternative approaches to selecting a valid RSC value. We ask that his report be considered to be part of these comments.

Response: See response to comment code 5210.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group (PSG)
EPA Document ID: EPA-HQ-OW-2007-0068-0168
EPA Comment ID: 20281
EPA Comment Code: 5210

Comment: BIOMONITORING DATA SUGGESTS THERE IS NO NEED TO ACCOUNT FOR PERCHLORATE EXPOSURES FROM OTHER SOURCES

In the absence of extensive biomonitoring data, EPA has historically created an HRL by multiplying the Drinking Water Equivalent Level (DWEL) of the RfD by a Relative Source Contribution (RSC) for the constituent (a factor of the proportion of exposure expected to come from water). EPA's Support Document outlines several options that EPA suggests for its RSC determination using the biomonitoring data and food surveys. If performed in a scientifically valid manner, the data shows that EPA would calculate an RSC of one (which yields an HRL of 24.5 ppb drinking water equivalent).

EPA also references other approaches to calculate the RSC that appear to be at variance with the best available scientific information, representing overly conservative departures from customary EPA policy or apparently requiring months of additional computations.

Ultimately, it appears that these approaches would yield essentially the same result: an RSC of one, which would render them duplicative.

Attachment 3 [See PDF of docket ID EPA-HQ-OW-2007-0068-0168] provides detailed exploration of the issues raised in this section. Our analysis finds that proper application of the best available science through any of the Agencysuggested approaches will yield the same conclusion - perchlorate in drinking water is a small fraction of total exposure. Using the most reliable of the approaches EPA outlines, the RSC factor is essentially equal to one.

Response: See response to comment code 5210.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20959
EPA Comment Code: 5210

Comment: Checking some outcomes from the current EPA HRL determination exercise

-Apart from the above considerations, the EPA RSC derived from the FDA TDI study seems to correspond fairly well with the average perchlorate drinking water levels found in the U.S.

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20961
EPA Comment Code: 5210

Comment: Additionally and apart from this, the EPA RSC has been checked against estimated average perchlorate dietary uptake via drinking water (section 3.1.)

Also the EPA HRL has been checked against the HRL obtained the conventional way but with additional available data integrated (section 3.2.)

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20964
EPA Comment Code: 5210

Comment: 1.2. The dose-response trial set-up

For clinical dose-response trials similar to the Greer trial, there are 3 possible trial set-ups.

1.2.1. Trial set-up type 1 leading to RSC < 1

The NOEL and therefore the RfD are based on a dose-response trial without food and without drinking water background level contribution.

Or in other words the subjects that are administered the doses have a perchlorate free food diet and drink purified water.

Therefore to arrive at the HRL the food background (FBG) level in the population will have to be estimated and subtracted from the RfD(which is based on the NOEL) . Therefore the RSC < 1 i.e. not all the RfD is attributed to DW.

Example:

Note: The examples are for illustrative purposes only. An UF of 4 is applied to allow smaller figures.

NOEL1= 10ug/kg-day. RfD1 =2.5ug/kg-day

The FBG contains 1.25 ug/kg-day (0.5 or 50% of RfD). Thus the part of the RfD attributed to DW is 0.5 RfD or 50 % of the RfD.

HRL1= maximum level of contaminant that DW should contain = [(RfD1 Ã— BW) /DWI] Ã— RSC=2.5 x70/2x0.5= 43.75 ppb.

Fig.1: NOEL based on dose-response trial without perchlorate food /drinking water background: RSC [see PDF Docket ID EPA-HQ-OW-2008-0692-1798]

1.2.2. Trial set-up type 2 leading to RSC=1

The NOEL and therefore the RfD are based on a dose-response trial with food background (FGB) and without drinking water background (DWBG) level contribution.

Or in other words the subjects that are administered the doses have a food diet with perchlorate background but drink purified water.

Therefore to arrive at the HRL, the FBG level in the population is already included in the NOEL and thus does not have to be estimated and not subtracted from the RfD. Therefore RSC = 1 or 100% i.e. all of the RfD is attributed to DW.

The effective NOEL2 is larger than the dose NOEL1.

Example: NOEL1 = 10ug/kg-day. FBG= 1.25 ug/kg-day. NOEL2 = NOEL1 + FBG=10 + 1.25 = 11.25 ug/kg-day.

RfD2 =1.125 ug/kg-day.

The food diet background as mentioned has already been accounted for.

The part of RfD2 attributed to water is 1 or 100 % of RfD2.

HRL2 = [(RfD2Ã— BW) /DWI] Ã— RSC=1.125 x70/2x1 = 39.4 ppb.

Or in other words, since NOEL1 is a dose added on top of the food background (see fig. 2) the whole RfD is attributed to DW.

Fig. 2: NOEL based on dose-response trial with perchlorate food background and without drinking water background: RSC = 1 [see PDF Docket ID EPA-HQ- OW-2008-0692-1798]

1.2.3. Trial set-up type 3: RSC is arithmetically >1

The NOEL and therefore the RfD are based on a dose-response trial with food background and with drinking water background level contribution.

Or in other words the subjects that are administered the doses have a food diet with perchlorate background and drink already contaminated water.

Since the NOEL1 is added on top of the food background (see drawing), the whole RfD is attributed to DW.

Now, the DW background (DWBG) itself is on top of the NOEL1 .Therefore, arithmetically, the RSC must be <1.

Example 1: NOEL1 = 10ug/kg-day. FBG= 1.25 ug/kg-day. DWBG = 0.625 ug/kg-day. NOEL3= NOEL1 + FBG +DWBG=10 + 1.25 +0.625 = 11.9 ug/kg-day. RfD3 =1.19 ug/kg-day.

HRL3 = [(RfD2 +DWBG) Ã— BW)/DWI] Ã— RSC= [(RfD3 Ã— BW)/DWI] Ã— RSC= (1.19 x70/2) x1 = 41.65 ppb.

Example 2: Assume perchlorate 1.5 ppb DW background and NOEL2 =0.7 ug/kg-day.

1.5 ppb background DW= 1.5 /70 x2= 0.04 ug/kg-day and HRL3 = (0.7+0.04) x 70 /2 x1 =26 ppb which arithmetically comes down to an RSC of 1.04 as 0.74x70/2 x 1.04= 26 ppb as well.

Fig. 3: NOEL based on dose-response trial with perchlorate food background and with drinking water background: RSC > 1 [see PDF Docket ID EPA-HQ- OW-2008-0692-1798]

More considerations about the RSC and practical examples can be found in: http://oehha.ca.gov/water/reports/howdsot.html.

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20972
EPA Comment Code: 5210

Comment: 3.1. RSC check

If the contribution from food would be 10% (see EPAâ€™s table 8) and which is derived from the TDS study model then of the 0.04 ug /kg-day total average perchlorate background exposure, 0.036 ug /kg-day would come from water.

Even, as already noted above, this is low compared to the other goitrogens, it would still translate into a US average drinking water content of 1.3 ppb (0.036 x70/2) which appears somewhat high but still close to EPAâ€™s data on U.S. wide DW perchlorate levels. Therefore the TDS model may be an accurate enough tool to estimate RSCs.

Response: See response to comment code 5120 for a discussion of the relative source contribution.

Commenter Name:
Commenter Organization: Ag Council et al
EPA Document ID: EPA-HQ-OW-2008-0692-1987
EPA Comment ID: 20977
EPA Comment Code: 5210

Comment: EPA's Calculation of the Relative Source Contribution for its Preliminary Determination also Reveals that the Food Contribution is Below the Level of Concern.

The US Centers for Disease Control's National Health and Nutrition Examination Survey (NHANES) biomonitoring data provides a superior measure of actual human exposure to perchlorate from all sources, including food and water. FDA's TDS and food sampling data, which provides an approximation of human exposure to perchlorate from food, in fact validates EPA's calculation of the relative source contribution from food.

Response: See response to comment ID 28919 under comment code 5210.

Commenter Name: Kate Sande
Commenter Organization: Minnesota Department of Health, Health Risk Assessment Section
EPA Document ID: EPA-HQ-OW-2009-0297-0663
EPA Comment ID: 28703
EPA Comment Code: 5210

Comment: Relative Source Contribution (RSC) MDH acknowledges the extensive national database of perchlorate exposure information that includes perchlorate concentrations found in food and beverages as well as biomonitoring data. We understand EPA's use of the NHANES biomonitoring data to estimate the 90th percentile food dose for pregnant women leading to the derivation of the drinking water RSC. For infants and young children, EPA states that the RSC is based on the central tendency dietary perchlorate exposure derived from FDA's Total Diet Study. MDH does wonder whether an RSC based on average dietary perchlorate exposure will protect individuals who have higher dietary doses. However, EPA's RSC for children 12- months and younger (0.59) based on the central tendency exposure is not much higher than the default RSC used by MDH for infants (0.5).

MDH uses 0.2 as the relative source contribution (RSC) default value for volatile chemicals for all exposure durations. However, for non-volatile chemicals, an RSC of 0.5 is used for acute and short-term exposure durations and 0.2 is used for subchronic and chronic exposure durations.

Response: See response to comment code 5210. EPA believes that the central or mean estimates of dietary intake of perchlorate from the total diet study are the best available peer reviewed data for determining the relative source contribution.

Commenter Name: Danielle Blacet
Commenter Organization: Association of California Water Agencies
EPA Document ID: EPA-HQ-OW-2009-0297-0208
EPA Comment ID: 28919
EPA Comment Code: 5210

Comment: 2) Exposure from other sources

The best evidence to date suggests that perchlorate is ubiquitous in the United States but UCMR data and other research suggest that little of this exposure is via drinking water. In addition, USEPA used the Greer et al study that used individuals who did not control or measure their exposure to perchlorate from food, a major source of perchlorate. This means that the ubiquitous background of perchlorate exposure found in the United States was built into the study, which was measuring the

effect of additional exposure above the background. This, along with the use of the no observed effect level (NOEL) versus no observed adverse effect level (NOAEL), actually makes the study more robust and has additional protection built into it. When the USEPA later uses uncertainty factors in their review, they are double-counting those factors.

The use of a relative source contribution (RSC) does not appear to be warranted in this situation. Given the very small contribution to perchlorate exposure from drinking water, the precedent set by USEPA when they evaluated sodium was that the RSC should be ignored. It is also important to note that other more dominant goitrogens have much greater occurrence than perchlorate in drinking water.

Response: See response to comment code 5210 for a discussion of the RSC.

EPA does not believe the conditions for the sodium regulatory determination are comparable to those for perchlorate. Dietary exposure alone does not exceed the reference dose; however, for some people in water systems with perchlorate contamination the dietary exposure combined with drinking water exposure may result in a total dose that exceeds the RfD for perchlorate. This is of particular concern among sensitive life stages.

Commenter Name: Kay Brothers
Commenter Organization: Southern Nevada Water Authority
EPA Document ID: EPA-HQ-OW-2009-0297-0667
EPA Comment ID: 29076
EPA Comment Code: 5210

Comment: Furthermore, based upon available epidemiological and other human studies, the use of RSC is inappropriate. For these reasons, it is unlikely that modeling a compound known to form naturally and occur ubiquitously represents an appropriate representation of actual conditions.

Response: See response to comment code 5210.

EPA Comment Code: 5220 Derivation of the HRL

Response to Code 5220: EPA has reversed its October 2008 preliminary determination not to develop an NPDWR for perchlorate and now concludes, based on the analysis presented in today's notice, that perchlorate meets the criteria for regulating a contaminant in Section 1412(b)(1)(A) of SDWA. EPA has found that 1.) perchlorate may have an adverse effect on the health of persons; 2) perchlorate is known to occur or there is a substantial likelihood that perchlorate will occur in public water systems with a frequency and at levels of public health concern; and 3) in the sole judgment of the Administrator, regulation of perchlorate in drinking water systems presents a meaningful opportunity for health risk reduction for persons served by public water systems. In proposing a national primary drinking water standard, EPA will seek public comments on the proposed standard, and analyses on which it is based, pursuant to SDWA requirements.

EPA has made this determination by comparing the best available data on the occurrence of perchlorate in PWSs to potential health reference levels (HRLs) for perchlorate. HRLs are not final determinations about the level of a contaminant in drinking water that is necessary to protect any particular population. Rather they are benchmarks against which EPA compares the concentration of a contaminant found in public water systems to determine if it is at levels of public health concern.

In the October 2008 preliminary regulatory determination, EPA had derived a single HRL of 15 µg/L based upon the RfD, an estimate of perchlorate exposure from food for pregnant women, and traditional adult body weight (70 kg) and drinking water consumption (2 L/day) values. This single HRL was derived to reflect exposure to a pregnant woman and her fetus, which the NRC identified as "the most sensitive population."

Since the NRC also identified infants and developing children as additional life stages, EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 µg/L to 47 µg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These HRLs are calculated based on individuals who consume an average amount of perchlorate from food (except for pregnant women where EPA used a 90th percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts.

EPA is evaluating these potential alternative HRLs and considers them to be levels of public health concern for purposes of this determination. EPA has compared these values to the data provided by PWSs subject to the first Unregulated Contaminant Monitoring Rule (UCMR 1). EPA collected and analyzed drinking water occurrence data for perchlorate from 3,865 PWSs between 2001 and 2005 under the UCMR 1. The minimum reporting level (MRL) for perchlorate under the UCMR 1 was 4 µg/L.

EPA found that 160 (approximately 4.1 percent) of the 3,865 PWSs that sampled and reported had at least 1 analytical detection of perchlorate (in at least 1 sampling point) at levels greater than or equal to the MRL of 4 µg/L. Table 1 of today's notice presents the number and percentage of PWSs

that reported perchlorate at levels exceeding various threshold concentrations. Note that the MRL for perchlorate under the UCMR 1 was 4 μg/L.

Given the range of potential alternative HRLs, EPA has reversed its October 2008 preliminary determination not to regulate perchlorate in drinking water. Based on the data in Table 1 and the range of potential alternative HRLs, EPA has determined that perchlorate is known to occur or there is a substantial likelihood that it will occur with a frequency and at levels of public health concern.

Table 2 of today's notice presents EPA's estimates of the population served by PWSs that were monitored under UCMR 1 for which the highest reported perchlorate concentration was greater than the thresholds identified in Table 1. These population estimates are for people at all life stages. EPA has determined that a NPDWR for perchlorate could reduce perchlorate exposures for these populations to levels below the potential alternative HRLs that EPA has identified as levels of public health concerns for purposes of this determination, and that such exposure reductions present a meaningful opportunity for the reduction of health risks for persons served by PWSs.

Individual Comments
Commenter Name: Apparent Mass Mailing #2 - Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-0100
EPA Comment ID: 19690
EPA Comment Code: 5220

Comment: The maximum safe level for perchlorate in drinking water is now 15 times higher than what the EPA declared safe in 2002. Under this new standard, more than 16 million Americans are exposed to unsafe levels of perchlorate in their drinking water, and independent analysis shows anywhere from 20 to 40 million Americans at risk. Perchlorate has been found in the drinking water in 35 states in the U.S.

Response: See response to comment ID 19873 under comment code 5220.

Commenter Name: Apparent Mass Mailing #2 - Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-0100
EPA Comment ID: 19690
EPA Comment Code: 5220

Comment: The maximum safe level for perchlorate in drinking water is now 15 times higher than what the EPA declared safe in 2002. Under this new standard, more than 16 million Americans are exposed to unsafe levels of perchlorate in their drinking water, and independent analysis shows anywhere from 20 to 40 million Americans at risk. Perchlorate has been found in the drinking water in 35 states in the U.S.

Response: See response to comment ID 19873 under comment code 5220.

Commenter Name: A. Lane
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0276
EPA Comment ID: 19781

EPA Comment Code: 5220

Comment: According to the EPA's own data, 16 million Americans are at risk of being exposed to Perchlorate. The maximum safe level for perchlorate in drinking water is now 15 times higher than what the EPA declared safe in 2002.

Response: See response to comment ID 19873 under comment code 5220.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0422
EPA Comment ID: 19873
EPA Comment Code: 5220

Comment: Please follow our own Environmental Protection Agency's recommendations for levels of perchlorate allowed in drinking water, set in 2002. Thank you.

Response: EPA's 2002 draft risk assessment was revised based upon the 2005 National Research Council's (NRC) recommendations. EPA has developed potential health reference levels (HRLs) for perchlorate for purposes of this regulatory determination. HRLs are not final determinations about the level of a contaminant in drinking water that is necessary to protect any particular population. Rather they are benchmarks against which EPA compares the concentration of a contaminant found in public water systems to determine if it is at levels of public health concern.
See response to comment codes 5220 and 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0475
EPA Comment ID: 19903
EPA Comment Code: 5220

Comment: The maximum safe level for perchlorate in drinking water is now 15 times higher than what the EPA declared safe in 2002. Under this new standard, more than 16 million Americans are exposed to unsafe levels of perchlorate in their drinking water, and independent analysis shows anywhere from 20 to 40 million Americans at risk. Perchlorate has been found in the drinking water in 35 states in the U.S.

Response: See response to comment ID 19873 under comment code 5220.

Commenter Name: S. G. Gompf
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0490
EPA Comment ID: 19911
EPA Comment Code: 5220

Comment: Since 2002, the EPA's maximum safe level for perchlorate in drinking water raised 15-fold! Why was the bar lowered? As an American mother and a physician, I have to question why the

EPA appears to be acting against the interests of its constituents in thismatter, and whether the EPA is acting in the interest of hidden benefactors in industry.

Response: See response to comment ID 19873 under comment code 5220.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0493
EPA Comment ID: 19915
EPA Comment Code: 5220

Comment: Millions of Americans in over 35 states are exposed to this chemical as maximum safe level for perchlorate in drinking water is now 15 times higher than what the EPA declared safe in 2002. PSR 2008.

Response: See response to comment ID 19873 under comment code 5220.

Commenter Name: A. L. Segall
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0506
EPA Comment ID: 19926
EPA Comment Code: 5220

Comment: I understand that the amount of perchlorate in our drinking water is now 15 times the amount that the government determined was safe in 2002. It seems clear that we should not allow such a large amount of this chemical to be in our drinking water.

Response: See response to comment ID 19873 under comment code 5220.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0525
EPA Comment ID: 19938
EPA Comment Code: 5220

Comment: Please renew the 2002 EPA Standards concerning Perchlorate. It is in the Nations best interest.

Response: See response to comment ID 19873 under comment code 5220.

Commenter Name: K. Peterson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0646
EPA Comment ID: 19989
EPA Comment Code: 5220

Comment: It is unacceptable that the maximum safe level for perchlorate in drinking water is now 15 times higher than what the EPA declared safe in 2002. How does that happen? This is a huge

defeat for the environment and for public health; it would be laughable if it wasn't such a serious issue.

As the Environmental Protection Agency, you are supposed to be protecting the environment and public health. If you are going to raise your "maximum safe level" for perchlorate, why don't you just go ahead and change your name to the Chemical Companies' Protection Agency? That would be a much more suitable monkier for the actions you are taking.

Response: See response to comment ID 19873 under comment code 5220.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group (PSG)
EPA Document ID: EPA-HQ-OW-2007-0068-0168
EPA Comment ID: 20279
EPA Comment Code: 5220

Comment: REVIEW OF THE NAS REPORT AND SUBSEQUENT PEER-REVIEWED STUDIES AFFIRMS USE OF THE RfD AS THE HEALTH REFERENCE LEVEL

EPA must often make important decisions on the basis of less information than it would wish; and perchlorate is a welcome exception.

There is extensive scientific literature, most notably a comprehensive, authoritative review of the range of peer-reviewed studies by the National Research Council of the National Academy of Sciences (NAS). The success of EPA, along with other agencies, in obtaining this review has put the Agency in an unusually well-informed position, backed by the deliberations and judgment of the nation's highest scientific body. The NAS Report, followed by the Agency's own RfD process, is supplemented by subsequent, peer-reviewed studies. Taken together, these comprise a solid basis for an EPA regulatory determination.

EPA's RfD is the best health benchmark to use as the health reference level (HRL). EPA concurred with the conclusion of the NAS panel in the adoption of the panel's recommendation as EPA's RfD. This RfD is based on the NAS panel's emphatically conservative approach of establishing the point of departure at the No Observed Effect Level (NOEL), rather than EPA's customary No Observed Adverse Effect Level (NOAEL). Consistent with EPA's design for RfDs, the NAS panel selected its recommended RfD to be protective of all sensitive populations. Subsequent peer-reviewed studies affirm and reinforce the conclusion that the RfD is a conservative, health protective value that protects all members of society, even the most sensitive population.

Further discussion of these studies and our comments is contained in Attachment 1 [See PDF of docket ID EPA-HQ-OW-2007-0068-0168].

Response: EPA is utilizing the RfD to derive potential alternative health reference levels and evaluate the opportunity for health risk reduction through a drinking water regulation for perchlorate. See response to comment code 5220.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection

EPA Document ID: EPA-HQ-OW-2008-0692-1422
EPA Comment ID: 20431
EPA Comment Code: 5220

Comment: 2. EPA's HRL Is Not Sufficiently Health Protective. MassDEP continues to believe that EPA's Reference Dose (RfD) and the associated Health Reference evel (HRL) for drinking water for perchlorate are insufficiently health protective of neonatal exposures. There is compelling evidence to support a national drinking water standard for perchlorate at a value well below EPA's HRL of 15 ppb.

* Literature publications (Zoeller and Rice, 2004; Zoeller, 2006; Ginsberg et al., 2007) and state agency risk assessments (MassDEP, 2006; CA, 2004) support a more health protective RfD and drinking water value. EPA's HRL of 15 ppb is 7.5 times higher than MassDEP's drinking water standard of 2 ppb and 2.5 times higher than California's standard of 6 ppb. EPA's evaluation includes no discussion of these alternative assessments. * The results of Blount et al (2006) and Steinmaus et al (2007) demonstrate thyroid effects associated with a dose of 0.06 ug/kg/day in iodide insufficient women, which is well below, and calls into question the protectiveness of, EPA's RfD of 0.7 ug/kg/day. * Although acknowledged in EPA's evaluation, potential interactive effects between thiocyanate, a metabolite of cyanide found in tobacco smoke and some common foods, and perchlorate, were not accounted for. Such interactions heighten concern regarding perchlorate induced thyroid hormone effects in women with serum iodine levels < 100 ug/L. * Use of a more appropriate and health protective RfD would lower the acceptable drinking water limit for perchlorate, resulting in a substantial increase in the total number of citizens exposed to unacceptably high levels of this toxicant from drinking water. This would clearly create a "meaningful opportunity for health risk reduction" through a national perchlorate drinking water regulation under the Safe Water Drinking Act.

Response: See response to comment code 5220.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection
EPA Document ID: EPA-HQ-OW-2008-0692-1422
EPA Comment ID: 20432
EPA Comment Code: 5220

Comment: 3. Infant Exposures at the HRL Exceed EPA's Insufficiently Protective RfD. EPA's calculations (Table 8, Federal Register publication) demonstrate that perchlorate intake by nursing and bottle-fed infants and children to 2 years of age, attributable to the consumption of drinking water at 15 ug/L (and not even considering other dietary sources of exposure) would substantially exceed EPA's insufficiently health protective RfD value. Based on EPA's own calculations, a bottle-fed infant would receive a dose of perchlorate 5 times higher than EPA's RfD and 50 times higher than MassDEP's RfD. Consistent with EPA's assessment, in a study conducted in Texas Dasgupta et al. (2008) also showed that the majority the infants (9 out 13 infants) in their study ingested perchlorate at a level that exceeds the EPA reference dose. Furthermore, this study indicates that breast milk iodide concentrations decrease as perchlorate levels increase in breast milk (Dasgupta et al., 2008), potentially raising risks to nursing infants. Due to potential impacts on children's health, this data alone justifies the establishment of a lower, more appropriately health protective HRL for perchlorate. By discounting this information in the evaluation, EPA is de facto adopting an even

higher, less protective RfD for these sensitive subgroups. EPA's explanation for discounting these findings- that the model's predicted iodide uptake inhibition (IUI) level at 15 ppb would be insignificant- is unjustified for at least three reasons.

a. The predicted IUI in these groups is very uncertain due to model limitations.

b. Although EPA indicates that iodide uptake inhibition of 2.2% is non- adverse, no objective data exists to support this determination and no objective safe level of IUI, especially in the neonate, has been established. In fact, the Blount et al. (2006) and Steinamus et al. (2007) studies indicate that 2.6 ug/L of urinary perchlorate (which equates to an approximate dose level of 0.06 ug/kg/d in iodine deficient women was associated with decreased T4 and increased TSH levels, consistent with the mode of action of perchlorate. Iodide uptake inhibition at this dose level would be predicted by the model to be very small suggesting either that the model is inaccurate; the effect is not solely due to IUI or low levels of IUI are adverse.

c. Allowing up to 2.2% iodine uptake inhibition also exceeds NRC's hypothesized non-adverse effect level of 1.8% IUI (NRC, 2005) although 1.8% IUI is considered an adverse effect level by many scientists (US EPA 2002; Ginsberg and Rice, 2005; and MassDEP, 2006).

Response: See response to comment code 5220 for a discussion of the alternative Health Reference Levels. Regarding the predictions of iodide uptake inhibition Physiologically-Based Pharmacokinetic (PBPK) Modeling , EPA reviewed, modified, and applied the perchlorate PBPK models, which were originally developed by Merrill et al. (2005) for adults and Clewell et al. (2007) for other life stages, to estimate the iodide uptake inhibition in the thyroid for each life-stage (73 FR 60262; USEPA 2008a). Estimated ingestion rates were then used to estimate the internal dose and resulting iodide uptake inhibition for several life stages, including susceptible populations (e.g., pregnant women and their fetuses, as well as breast-fed and bottle-fed infants).

In the August 2009 notice, EPA stated that it was re-evaluating how best to incorporate the PBPK modeling analysis into its evaluation of perchlorate- if at all. The Agency sought comments on ways to use the PBPK modeling analysis to inform the regulatory determination.

Several commenters support the use of the PBPK model to inform the regulatory determination only if the significant limitations of the current model are addressed. For example, the inability of the model to reflect iodide nutritional status was cited by commenters and three of the four peer reviewers as an important limitation. Also, several commenters stated that the risks to breast-fed infants and young children are not adequately addressed. They challenged that the modeling analysis is based on average weight infants and healthy adults, while the sensitive life stages for perchlorate include premature infants and hypothyroid women.

After further consideration of the peer review and public comments, EPA concludes that the PBPK modeling analysis, in the context of the perchlorate regulatory determination, is useful in examining which life stages are most susceptible to the effects of perchlorate. For example, the model indicates that a fetus may be seven times more sensitive to the effects of perchlorate than a pregnant woman. The model also allows for the estimation of the concentration of perchlorate in breast milk (thus breast-fed infant exposure) at various maternal perchlorate exposure levels. However, because of the stated limitations, EPA has decided the model does not directly bear on the current decision

regarding the need for a NPDWR for perchlorate. EPA is continuing to evaluate whether the model could be used in setting a NPDWR for perchlorate.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Dept. of Environmental Protection
EPA Document ID: EPA-HQ-OW-2008-0692-1526
EPA Comment ID: 20449
EPA Comment Code: 5220

Comment: Further, it is our opinion that the information provided in the proposal indicates that 15 ug/L is not a health protective drinking water concentration, and that the HRL should be set at a lower level that is protective of public health for all exposed subpopulations. A primary concern is that the exposure and health risks of bottle-fed infants, as predicted by the PBPK model, are ignored in the proposal. The PBPK model predicts that when the perchlorate concentration in water used to prepare formula is 15 ug/L, 7-day and 60-day old bottle-fed infants are exposed to more than 5 times the RfD, and that iodide uptake in 7-day old infants is decreased by 2.2% (Table 8). Even if the model were to use the median rather than the 90th percentile water intake, the RfD would be greatly exceeded. The model also predicts that a breast-fed infant would be exposed to more than twice the RfD from perchlorate in the mother's milk due to maternal ingestion of water contaminated with 15 ug/L perchlorate. The weaned 6-12 month old is predicted to be exposed to almost 3 times the RfD when water with 15 ug/L perchlorate is used to prepare fluids and foods.

Response: See response to comment code 5220 and response to comment ID 20432 under comment code 5220.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Dept. of Environmental Protection
EPA Document ID: EPA-HQ-OW-2008-0692-1526
EPA Comment ID: 20451
EPA Comment Code: 5220

Comment: Decision not to regulate perchlorate based on population exposed above the HRL

The estimation of the number of people exposed to perchlorate at a level of public health concern in public drinking water is determined by the perchlorate concentration chosen as the HRL. Setting an HRL at an inappropriately high concentration, 15 ug/L, greatly reduces the size of the population predicted to be exposed at a level of public health concern. Table 2 of the proposal shows that approximately 2 million people (in 0.8% of systems) or, alternatively, an estimated 0.9 million people served by 0.29% of points-of-entry (POEs) are exposed at or above an HRL of 15 ug/L. USEPA states that this number of people is not sufficient to warrant regulation. However, if the level were to be set at 5 ug/L, for example (a concentration that still would result in bottle-fed infants being exposed slightly above the Reference Dose, based on the exposure assumptions in Table 8), 5 to 7 times more individuals would be exposed above the HRL than at 15 ug/L: 14.6 million people (3.2% of systems) or 4 million people served by 1.9% of POEs would be exposed above 5 ug/L. Therefore, by setting the drinking water concentration higher than it should be from a health viewpoint, USEPA has also significantly minimized the need for regulation of perchlorate from an occurrence viewpoint.

Response: See response to comment code 5220.

Commenter Name: Gregg Grunenfelder
Commenter Organization: Washington State Department of Health; and Oregon Department of Human Services
EPA Document ID: EPA-HQ-OW-2008-0692-1529
EPA Comment ID: 20459
EPA Comment Code: 5220

Comment: * Roughly, 17% of reproductive-aged women in the United States are especially susceptible to perchlorate toxicity due to inadequate dietary intake of iodine and are susceptible to hypothyroxinemia and hypothyroisism during pregnancy. There is a possibility that some women in the child-bearing age in the United States are getting less than the recommended daily iodide intake level.

* Iodine deficiency during early pregnancy may cause irreversible neurodevelopmental deficits in offspring.

* Exposure to perchlorate is likely to further reduce iodide uptake by the thyroid.

* As many as 350,000 pregnant women within the United States may be exposed at any given time to perchlorate levels considered unsafe.

Because there is uncertainty regarding our understanding of perchlorate toxicity, exposure, and presence in the environment, a cautious approach for protecting sensitive populations should be taken. The department concludes that EPA's health reference level is not adequately protective of the health of sensitive subpopulations and the determination that a meaningful opportunity for risk reduction through the regulation of perchlorate in drinking water is not supported from a public health perspective.

Response: See response to comment code 5220.

Commenter Name: Denise F. Sipple
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1621
EPA Comment ID: 20548
EPA Comment Code: 5220

Comment: Many experts disagree with your assessment that drinking water with 15 parts per billion of perchlorate is safe and acceptable. Scientists from the California Environmental Protection Agency and the Massachusetts Department of Environmental Protection have set stricter standards to will ensure that the most vulnerable populations -- pregnant women, infants, and small children -- are protected from the adverse impacts of perchlorate.

EPA's analysis fails to consider that the combination of food and drinking water exposure to perchlorate in the U.S. population exceeds the reference dose set by EPA. Nor does it incorporate the more protective methodology behind the recent state regulatory actions. These flaws must be

remedied for the sake of the millions of U.S. families exposed to dangerous levels of perchlorate contamination.

Thank you and God Bless.

Response: See response to comment code 5220.

Commenter Name: Dick Wilson
Commenter Organization: Anaheim Public Utilities Department
EPA Document ID: EPA-HQ-OW-2008-0692-1530
EPA Comment ID: 20556
EPA Comment Code: 5220

Comment: Dear US EPA,

As a community water system in the State of California, Anaheim Public Utilities believes that continuing the process for establishing a drinking water standard for perchlorate would fall well within SDWA guidelines. Although the Preliminary Regulatory Determination on Perchlorate finds that a health reference level of 15 ug/l appears to be a reasonable estimate for a potential drinking water standard, the States of California and Massachusetts have established drinking water standards for perchlorate at much lower levels. Therefore, we conclude that there is ample evidence that the actual level of public health concern for perchlorate is truly much lower than the health reference level mentioned in the Preliminary Regulatory Determination.

Thank you for your consideration of this comment. Sincerely,

Dick Wilson Environmental Services Manager Anaheim Public Utilities Department 714-765-4277 dwilson@anaheim.net

Response: See response to comment code 5220.

Commenter Name: Robert Howd
Commenter Organization: California Environmental Protection Agency, Water Toxicology Section
EPA Document ID: EPA-HQ-OW-2008-0692-1671
EPA Comment ID: 20648
EPA Comment Code: 5220

Comment: IV (B), p 60275. The formula used to calculate the health risk level for perchlorate uses the default body weight for an adult male, and default drinking water consumption of 2 L/day. Recent EPA exposure assessment guidance (U.S. EPA, 2004) recommends using exposure data more relevant to the actual persons at risk. OEHHA has accepted that guidance in its risk assessments and is disappointed that EPA itself has not. Specifically, since the greatest risk of exposure to perchlorate appears to be in pregnant women and in infants, we believe that body weights and drinking water consumption values which are fully protective of these groups should be utilized in this risk assessment. The upper 95th percentile drinking water consumption rates appear to us to be adequately protective. Applying this health-protective value to the EPA reference dose of 0.7 ug/kg-day and relative source contribution of 0.62 yields the following:

Pregnant women: (0.0007 mg/kg-day x 0.62) / 0.055 L/kg-day = 0.008 mg/L

For infants, the comparable calculation is more complicated, because the reference dose of 0.7 ug/kg-day was calculated for an adult, as was the relative source contribution. However, if those values were retained, the following result is obtained:

Infants: (0.0007 mg/kg-day x 0.62) / 0.221 L/kg-day = 0.002 mg/L

If the starting point for calculation of the RfD were the BMDL of 0.0037 mg/kg- day, these numbers would be correspondingly lower, although again, a health- protective dose and relative source contribution for infants should be calculated separately. It seems to us that numbers in this range should be being used in making the decision whether or not to regulate perchlorate in drinking water.

IV (B)(3), p 60277. Table 7, Health Reference Levels for Pregnant Women. We are concerned that EPA continues to use the obsolete default values of 70 kg for body weight and 2 L/day of water consumption when these values certainly do not apply to pregnant women. These defaults are specifically intended for the population in general, and should be superseded by more specific and appropriate values when a risk assessment is being conducted for a defined subpopulation (U.S. EPA, 2004, 2005).

Response: See response to comment code 5220.

Commenter Name: Tim Cranford
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1896
EPA Comment ID: 20781
EPA Comment Code: 5220

Comment: Perchlorate has been linked to thyroid problems in vulnerable segments of our population, such as newborns, pregnant women and young children. The current "safe" levels of this chemical for drinking water is now set at some 15 times higher than was set in 2002.

Response: See response to comment ID 19873 under comment code 5220.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1983
EPA Comment ID: 20821
EPA Comment Code: 5220

Comment: The facts are that the maximum safe level for perchlorate in drinking water is now 15 times higher than what was declared safe in 2002. Under this new standard, more than 16 million Americans are exposed to unsafe levels of perchlorate in their drinking water, and independent analysis shows anywhere from 20 to 40 million Americans at risk. Perchlorate has been found in the drinking water in 35 states in the U.S.

Response: See response to comment ID 19873 under comment code 5220.

Commenter Name: Lee Walsh
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1997
EPA Comment ID: 20832
EPA Comment Code: 5220

Comment: It is absolutely outrageous that the allowable level of known toxin Perchlorate be increased by 1500% in the drinking water of the American people. At what benefit? What purpose can this possibly serve, to deliberately poison our own people?

Lee Walsh Albuquerque, NM

Response: See response to comment ID 19873 under comment code 5220.

Commenter Name: Mary Moore
Commenter Organization: Lindon Park Neighborhood Association (LPNA)
EPA Document ID: EPA-HQ-OW-2008-0692-2002
EPA Comment ID: 20834
EPA Comment Code: 5220

Comment: A more thorough investigation of the potential impact of perchorlate on fetuses, children and women seems appropriate. Even the model currently employed by EPA appears to propose a health reference level that exposes young children to perchlorate levels above the reference dose.

Response: See response to comment code 5220.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20915
EPA Comment Code: 5220

Comment: EPA's flawed assessment still finds that millions of people are exposed to potentially harmful levels of perchlorate: EPA's assessment is fundamentally flawed for the reasons described above. In this assessment, EPA determines that 15 ug/L (15 ppb) is an appropriate health reference level (HRL); this number was arrived at, in part, by using data from the unpublished study that was just described in the preceding section of this document. It should be noted that in the Blount study, women with lower iodine levels who had exposure to perchlorate in drinking water as low as 2 ppb had an associated 11% decrease in thyroid hormone levels (Blount et al. 2006b). It is clear that the EPA HRL is not protective of public health since levels of perchlorate exposure far below 15 ug/L result in significant changes in thyroid hormone levels.

Response: See response to comment code 5220.

Commenter Name: Caroline Baier-Anderson, PhD

Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20951
EPA Comment Code: 5220

Comment: EPA concludes that a health risk level (HRL) of 15 ug/L would be adequate to protect public health. We strongly disagree. As documented in the previous sections, the HRL is based on a flawed reference dose, and does not adequately take into account either the role of individual variability or iodine status factors that recent studies have demonstrated play a critical role in determining an individual's response to perchlorate. When combined with what is known about the biology of thyroid homeostasis and the increased sensitivity of the fetus and neonate, it is clear that the HRL will not adequately protect sensitive subpopulations in the US.

Response: See response to comment code 5220.

Commenter Name: Caroline Baier-Anderson, PhD
Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20953
EPA Comment Code: 5220

Comment: Determining the number of facilities where perchlorate concentrations exceed a health-protective level depends on the selection of a health-protective level; as a result of this circular logic, if the health risk level is under- protective, then a smaller number of facilities will be identified. A lower, more protective health risk level will identify a larger number of facilities, and therefore exposed individual. As we have documented in the previous sections, the health risk level selected by EPA is not adequate to protect sensitive subpopulations. Hence, EPA underestimates the number of facilities that are supplying perchlorate-contaminated drinking water.

Response: See response to comment code 5220.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20956
EPA Comment Code: 5220

Comment: Summary

1. When to apply a RSC and when not

Applying a RSC when determining the HRL for perchlorate is not justified as the NOEL found thru the clinical dose-response trial on which the HRL is based already incorporates a RSC thru the background level that was present.

Response: See response to comment code 5210.

Commenter Name: Herwig Opdebeeck

Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20958
EPA Comment Code: 5220

Comment: -Consequently, to be health protective, a joint DW HRL of nitrate and perchlorate of 45 ppb total perchlorate equivalent should be proposed.

-If for nitrate the same UF=10 would be applied as for perchlorate, the HRL for perchlorate alone, after subtraction of this adjusted nitrate MCL would be 26.7 ppb which is close to the 27 ppb derived from the total perchlorate equivalent RfD when attributing a 40% share of nitrate plus thiocyanate in this goitrogenic background conform with the NHANES data. It is also close to the current EPA DWEL of 24.5 ppb.

Consequently those 2 alternative data based approaches seem to confirm once more the NRS RfD and the current EPA DWEL based on a RSC of 1.

Response: While EPA acknowledges that nitrate and thiocyanate have the same mode of action as perchlorate, and that the effects of combined exposure to perchlorate, nitrate, and thiocyanate are additive, EPA does not believe there are sufficient scientific data currently available to assess and characterize the combined risk of these contaminants. EPA has committed to a drinking water strategy that outlines four principles to expand public health protection for drinking water (USEPA, 2010b). One of these principles is to address contaminants as groups. However, EPA does not believe that regulatory action to address perchlorate should be further delayed. Therefore, EPA is developing a proposed rule for perchlorate. Once the perchlorate standard is promulgated, EPA is required to review and revise, as appropriate, its drinking water standards at least every six years. Any revision must at least maintain or improve public health protection. When there are sufficient scientific data to assess the cumulative risks of perchlorate and other contaminants, EPA will review this information to evaluate whether any revisions of NPDWRs are appropriate.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20960
EPA Comment Code: 5220

Comment: -Also the PBPK model used by EPA arrives at a HRL that closely matches the one obtained by using the total perchlorate equivalent level and applying an RSC =1.

Because food exposure data and other relevant variables were recently available including for the most sensitive subpopulations, EPA chose to use a refined approach rather than EPAâ€™s former "default" approach to estimate the RSC leading to the HRL. However it may be useful to compare this HRL and the HRL that would have been obtained by using the former "default" RSC approach particularly when adding additional considerations and evidence not taken into account neither by the former not by the latter approach.

Response: See response to comment code 5220 for a description of the potential alternative HRLs and comment code 5210 for a discussion of the RSC.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20962
EPA Comment Code: 5220

Comment: 1. Determination of HRL applying an RSC or not

1.1. Introduction

(Note: from hereon we specify the NOEL, RfD and HRL as NOEL1,NOEL2 ,NOEL3 and NOEL4 ;RfD1,RfD2 ,RfD3 and RfD4 ;HRL1 , HRL2, HRL3 and HRL4 according to their subsequent specific meanings in this comment while with NOEL, RfD and HRL is meant their general meaning).

EPA bases its HRL for DW (drinking water) on the NRC (National Research Council) RfD (Reference Dose, 0.7ug/kg-day) according to the following equation:

HRL = [(RfD Ã— BW)/DWI] Ã— RSC with BW= Body weight = 70 kg and DWI = drinking water daily intake in litres.

Response: No response necessary to this summary of EPA information.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20966
EPA Comment Code: 5220

Comment: 2. The very particular case of perchlorate

Two particular considerations should be taken into account in determining a "state of the art" HRL for perchlorate besides the fact that the RSC should be equal to 1 and the fact that the full effective NOEL and RfD should be taken into account.

A. The background is known for perchlorate

To our knowledge this is the first time that background data are available that would allow to calculate an effective NO(A)EL for a contaminant for which a RSC is not needed to set a HRL.

Using the data and regression curves presented in Blount et al., (2006,b) (2) the average urinary perchlorate level of 2.84 ug/l (with a 95% confidence interval of 2.54-3.18 ug/l) translates into an average exposure or total background(food +DW) of around 0.04 ug /kg-day (which is 17times lower than the 0.7 ug /kg-day RfD).

The estimation of the effective Greer NOEL (NOEL3) is therefore still ? NOEL1 ? Âµg /kg-day. At first sight this is reassuring as it does not matter much if the background perchlorate would be

taken into account or not or whether the background food perchlorate level would have been subtracted already or not since NOEL3 is almost equal to NOEL1 meaning that also HRL3 would be almost identical to the HRL1 of 24.5 ppb.

It also shows that perchlorate background levels (food +DW) in the U.S. population are very low to start with as they represent only around 0.5 %(= 0.04/7) of the effective perchlorate NOEL3 and apparent perchlorate NOEL1 and 5% of the RfD.

Yet there is more to be considered.

Response: See response to comment code 5210 for a discussion of the RSC and comment code 5220 for a discussion of the potential alternative HRLs.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20969
EPA Comment Code: 5220

Comment: Yet, surprisingly, even though EPA refers to those goitrogens when discussing the Blount et al., (2006b) (2) biomonitoring study it does not take into account the available data that would allow it to significantly refine the RfD and the corresponding HRL.

If EPA would have done so, EPA would have found that the background level of the other goitrogens are, as noted, much more important than the one of perchlorate itself and should therefore been taken into consideration a priory. As mentioned the total perchlorate equivalent RfD should have been 1.28 ug/kg-day and the old DWEL of 24.5 ppb should be replaced by one of around 45 ppb for [perchlorate +nitrate /240].

The current MCL for nitrate is 44 ppm (10 ppm as nitrate) which translates into a 183 ppb perchlorate equivalent (44,000/240).

For Methemoglobinemia on which the nitrate MCL was based, a RSC of 1 and a UF of 1 was applied. A RSC of 1 was justified as explained above however an UF of 1 may, as suggested by CDC (9), or may not have been justified .However for nitrate to be as health protective for iodine uptake inhibition as the perchlorate RfD the same UF as perchlorate should have been applied when assuming that 44 ppm is a NOEL. On the contrary most probably 44 ppm is already above the NOEL (10).

In that case the new nitrate MCL would have an equivalent of 18.3 ppb perchlorate. This would then leave a HRL of 45 -18.3 = 26.7 ppb for perchlorate alone which, by the way, is close to the current EPA DWEL of 24.5 ppb.

Response: See response to comment ID 20958 under comment code 5220.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798

EPA Comment ID: 20971
EPA Comment Code: 5220

Comment: 3. A few checks of the current EPA approach in setting a HRL

As noted before, when, because of the trial set-up, the dose that allowed to determine a NOEL (or NOAEL) was not complementary to a background dietary level, the application of an RSC< 1 is necessary to come to a HRL for water only.

In that case most of the time a default RSC is used because of lack of more precise data. This makes the RSC an imprecise tool .Therefore a data based estimate such as the FDA TDS model used by FDA would, while still a model, have been an improvement.

However, as explained, trying to derive a HRL from the perchlorate RfD, applying an RSC<1 is not justified since the food contribution was already taken care of.

Yet the data on the perchlorate background and the total equivalent perchlorate background can be used to check the RSC based on the FDA TDS model and to check the EPA HRL based on the PBPK model

Response: See response to comment code 5210.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20973
EPA Comment Code: 5220

Comment: 3.2. HRL check

For the most sensitive population, as designated by EPA, and assuming a same nitrate and thiocyanate background intake as the Greer cohort , the perchlorate food dose for the highest 10% of this population segment is 0.26 ug/kg-day(see EPA table 6).

The (new) RfD that remains for DW would then be: 0.77-0.26 = 0.51 ug/kg-day which leads to a DW HRL of 17.8 ppb (0.51x70/2) which is close to the 15 ppb found by EPA for this sensitive group.

(1) Greer, M.A., G. Goodman, R.C. Pleuss, and S.E. Greer. Health effect assessment for environmental perchlorate contamination: the dose response for inhibition of thyroidal radioiodide uptake in humans. Environ Health Perspect. 2002. Vol. 110. pp. 927-937

(2) Blount, B.C., J.L. Pirkle, J.D. Osterloh, L. Valentin-Blasini, and K.L. Caldwell. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environmental Health Perspectives. 2006b. Vol. 114, No. 12. pp. 1865-1871.

(3) EPA, Office of Water , Office of Science and Technology, Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (EPA-822-B-00-004), 2000.

(4) Tonacchera M., Pinchera A., Dimida A., Ferrarini E., Agretti P., Vitti P., Santini F., Crump K., Gibbs J. Relative Potencies and additivity of perchlorate, thiocyanate, nitrate, and iodide on the inhibition of radioactive iodide uptake by the human sodium iodide symporter. Thyroid 14: 1012-1019. 2004.

De Groef B., Decallonne BR., Van der Geyten S., Darras VM., Bouillon R. Perchlorate versus other environmental sodium/iodide symporter inhibitors : potential thyroid-related health effects. European Journal of Endocrinology. 2006, 155: 17-25.

(5) Cardoso A. P., Ernesto M., Nicala D., Mirione E., Chavane L., Nâ€™zwalo H., Chikumba S., Cliff J., Mabota A. P. , Haque M. R., Bradbury J. H. Combination of cassava flour cyanide and urinary thiocyanate measurements of school children in Mozambique. International Journal of Food Sciences and Nutrition. May 2004. Volume 55, Number 3, 183-190

(6)Smith R. G., Malcom R. M. Urinary sulphur and thiocyanate excretion in cyanide poisoning. American Society for Pharmacology and Experimental Therapeutics. Journal of Pharmacology And Experimental Therapeutics. 1930. Vol. 40, Issue 4, 457-471, http://jpet.aspetjournals.org/cgi/content/abstract/40/4/457

(7) Florin T. H. J., Neale G., Cummings J. H. The effect of dietary nitrate on nitrate and nitrite excretion in man. MRC Dunn Clinical Nutrition Centre, 100 Tennis Court Road, Cambridge CB2 IQL. Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ. (Received 5 September 1989 - Accepted 11 May 1990.

(8) Vermeer I. T. M., Pachen D. M. F. A., Dallinga J. W. , Kleinjans J. C. S, van Maanen J. M. S. Volatile N-Nitrosamine Formation after Intake of Nitrate at the ADI Level in Combination with an Amine-rich Diet. Department of Health Risk Analysis and Toxicology, Maastricht University, The Netherlands. Environmental Health Perspectives. August 1998. Volume 106, Number 8.

(9) Manassaram D.M., Backer L. C., Moll D. M. A Review of Nitrates in Drinking Water: Maternal Exposure and Adverse Reproductive and Developmental Outcomes. Centers for Disease Control and Prevention, National Center for Environmental Helath, Health Sudies Branch, Atlanta, Georgia, USA. Environmental Health Perspectives. March 2006. Volume 114, number 3.

(10) TAJTAKOVA M.; SEMANOVA Z., TOMKOVA Z., SZÃ–KEOVA E., MAJOROS J., RADIKOVA Z., SEBÃ–KOVA E., KLIMES I., LANGER P. Increased thyroid volume and frequency of thyroid disorders signs in schoolchildren from nitrate polluted area. Chemosphere, ISSN 0045-6535 CODEN CMSHAF. 2006, vol. 62, no4, pp. 559-564 [6 page(s) (article)] (18 ref.).

RADIKOVA Z., TAJTAKOVA M., KOCAN A., TRNOVEC T., SEBÃ–KOVA E., KLIMES I., LANGER P. Possible Effects of Environmental Nitrates and Toxic Organochlorines on Human Thyroid in Highly Polluted Areas in Slovakia. Thyroid ISSN 1050-7256. 2008, vol. 18, no3, pp. 353-362 [10 page(s) (article)].

Response: See response to comment ID 20958 under comment code 5220.

Commenter Name: Jennifer Sass, PhD.

Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20985
EPA Comment Code: 5220

Comment: In simple terms, the HRL is the maximum contamination level of perchlorate that could be in drinking water, and still keep daily human consumption levels from exceeding the RfD of 0.7 ug/kg/day. EPA reports that for pregnant women, exposure to perchlorate from food is 0.263 ug/kg/day at the 90th percentile (based on data from a national food survey), representing nearly 38% of the RfD, thus leaving an RSC (Relative Source Contribution) for water of 62% (FR at 60276). This is equivalent to 0.437 ug/kg/day from water, assuming an average body weight of 70 kg, and a daily water consumption of 2 L (90th percentile adult water consumption). That is, 0.437 ug x 70 kg body wt. = 30.6 ug perchlorate in 2 L (the daily consumption amount). This is 15 ug/L, or 15 ppb, the HRL.

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 21007
EPA Comment Code: 5220

Comment: However, even if EPA proceeds with its determination not to regulate perchlorate and instead finalizes an HRL, that level must be adjusted to account for the actual data from the PBPK model showing that hundreds of thousands of infants would exceed the safe daily perchlorate intake levels at the proposed HRL.

These comments are respectfully submitted for your consideration,

Jennifer Sass, Ph.D. Mae Wu, JD

COMMENTS SUPPORTED BY THE FOLLOWING:

Center for Public Environmental Oversight a project of the Pacific Studies Center Lenny Siegel, Executive Director Mountain View, CA

Citizens for Safe Water Around Badger Laura Olah, Executive Director Merrimac, WI

Clean New York Bobbi Chase Wilding, Organizing Director Schenectady, NY

Concerned Citizens of the Plainview-Old Bethpage Community Inc. Carol Meschkow, President Plainview, New York

Environmental Health Fund Judith Robinson, Director of Programs Jamaica Plain, Boston

Greenpeace Rick Hind Washington, DC

Institute for Agriculture and Trade Policy David Wallinga, MD Minneapolis, MN

Natural Resources Council of Maine Matt Prindiville, Project Director Toxics and Sustainable Production Maine, USA

Physicians for Social Responsibility Evan Krasner, MD, Executive Director SF Bay Area Chapter

ScienceCorps Kathy Burns, Ph.D. Boston, MA

Response: See response to comment code 5220.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21058
EPA Comment Code: 5220

Comment: The EPA has determined that setting a NPDWR will not present a meaningful opportunity for health risk reduction based on assessments done by multiple authoritative scientific bodies, numerous well conducted human and animal experiments using a range of doses of perchlorate, and the occurrence and concentration of perchlorate in drinking water systems in the U.S. One of the rationales for this decision was the calculation of the HRL which was based on the RfD. The RfD combined this previous knowledge to determine a dose which is well above the threshold in healthy adults that does not cause inhibition of iodide uptake and dividing that dose by 10 to account for sensitive populations.

Response: See response to comment ID 20279 under comment code 5220.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21078
EPA Comment Code: 5220

Comment: III. IODINE SUFFICIENCY IN THE UNITED STATES

A significant degree of attention and concern related to perchlorate exposure has been focused upon the hypothetical iodine-deficient person. However, unless the doses of perchlorate are sufficient to significantly impair long term (not transient) iodide uptake, which would be considerably greater than 0.007 mg/kg-d (~240 ppb based on healthy adults; Greer et al. 2002), perchlorate exposure would not exacerbate iodine deficiency. As stated above, this dose was adjusted by an uncertainty ("safety") factor of 10. Thus, the approach used by EPA in deriving their HRL based on the RfD of 0.7 ug/kg-d, remains a conservative and health protective approach that accounts for substantial uncertainty. The NRC definitively states

"...a dose that does not inhibit thyroid iodide uptake will not affect thyroid function, even in subjects with an abnormal thyroid gland or a very low iodide intake."

There is concern that there are low iodine levels in the U.S. population. The concern is that low iodine levels in a pregnant woman for prolonged periods of time can cause a change in thyroid hormones that may affect the neurodevelopment of the fetus.

First and foremost, it is important to note that no study has demonstrated that exposure to environmentally-relevant levels of perchlorate causes or is associated with iodine deficiency. Taken at face value, Blount et al. (2006) show an association between thyroid disruptions and perchlorate; however, even if this association represented an actual biological effect at doses below the inhibition of iodine uptake, this hypothetical effect does not raise or lower the measured thyroid hormones outside of the normal ranges and do not show any adverse effect due to the exposure. An epidemiological study of chronically exposed populations in Chile, including children who were exposed throughout gestation via maternal exposure and in infancy through breastmilk and later dairy, show no adverse effects with exposure much higher than the RfD even with iodine intakes similar to that in the U.S. (Tellez et al., 2005).

Second, the TDS and NHANES both show that population intake of iodide exceed the recommended adequate intake for iodine (Murray et al., 2008; Blount et al., 2006). Although there have been questions regarding iodine sufficiency in the U.S., Borak (2005) points out that there has not been consistency regarding the application of WHO definitions of iodine insufficiency and interpreting the great variability in daily iodine levels (Borak, 2005). For instance, for a population to be considered iodine deficient by the WHO definition, the median urinary iodine concentration must be below 100 ug/L and at least 20% of the population must be below 50 ug/L. Borak notes that much of the confusion in the interpretation of NHANES data comes from this seemingly high number of people that may be below 50 ug/L urinary iodine. He explains "...the reason for such seemingly inconsistent criteria is the need to anticipate potentially large variability when iodine levels are measured in spot urine samples" (Borak, 2005).

Third, despite the presence of perchlorate in breast milk, studies have shown that this level of perchlorate does not cause adverse effects in children (Tellez et al., 2005; Amitai et al., 2007). Moreover, these studies have all shown doses of perchlorate that are below the NOEL from Greer et al. (2002), and are therefore insufficient to inhibit iodide uptake by the NIS. If a person, or a population, is iodine insufficient, reducing perchlorate, at environmental relevant concentrations, will not improve iodine insufficiency. Supplemental iodine will (e.g., iodized salt) reduce or negate iodine insufficiency.

Fourth, the NRC perchlorate panel concluded that iodide deficiency if it even exists in the U.S., is mild and "...perchlorate exposure most likely would not exacerbate it" (NRC, 2005). Finally, the RfD is a conservative health protective value that is based on a NOEL with the addition of a safety factor to account for the most sensitive individuals. The HRL, which is even more conservative than the RfD, was calculated based on pregnant women and was verified using PBPK modeling to consider whether the HRL would be protective of other sensitive subpopulations, including infants, by factoring in body weight, water intake, and food intake.

Response: The data underlying the definition of iodide uptake inhibition as a precursor effect and the relationship of iodide uptake inhibition to the continuum of adverse outcomes reflects an understanding of effects in adults; it may not reflect the relationship of the precursor event to adverse outcomes in neonates and infants, who may not have iodide stores sufficient to offset the effects of reduced iodide uptake. The less resilient neonatal and infant system makes the exposure

gap between a precursor event (iodide uptake inhibition due to perchlorate) and reduced T3/T4 levels likely to be narrower than for adults, and in fact, the distinction between the two may be blurred for the very young (Greer et al., 2002; Savin et al., 2003; van den Hove et al., 1999). The NRC noted that, "[T]he minimal prolonged decrease in thyroid hormone production that would be associated with adverse health effects is not known; any decrease is potentially more likely to have adverse effects in sensitive populations (people with thyroid disorders, pregnant women, fetuses, and infants) but data are not available to determine the magnitude of the decrease needed to cause adverse effects in those populations."
With regards to conclusions of the NRC panel on the effects of perchlorate exposure EPA believes the NRC appropriately based the RfD on iodide uptake inhibition to the thyroid, for the reasons discussed in its report.
See response to comment code 5220.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21098
EPA Comment Code: 5220

Comment: V. EPA's Methodology to Support the HRL Could be Explained More Completely

In the preliminary determination, EPA puts forth a methodology to measure the contribution of food to total exposure by combining two nationally- representative data sets. The best available scientific understanding supports EPA's use of actual data as opposed to default parameters to derive the RSC. As EPA set out in its 2007 notice, EPA has multiple options to estimate the contribution of food to total exposure. At that time, the PSG presented analysis of the scientific merits of these options. The conclusions in those comments remain valid: no matter which scientifically-valid approach EPA takes, EPA can and should conclude that a national drinking water standard would not yield a meaningful reduction in human health risk.

The approach outlined in the proposed determination and background document appears to have several limitations. These limitations may be omissions in the description and not in the methodology. While adequate to meet EPA's statutory obligation, we suggest that EPA's description could benefit from additional explanation. These suggestions are listed below.

* Sample Description. Both UCMR and NHANES are nationally representative samples. The sample frame and the sample weights are published and have undergone peer review. EPA takes a subsample from these data sets and compares them for its analysis. EPA's analysis could benefit from a more complete description of the characteristics of these subsamples. Further description would assist the public especially since EPA is comparing absolute levels of perchlorate measured in drinking water and in total exposure. Many factors could influence absolute amounts of food and drinking water consumption in a person at a given time such as climate, weight, age, and income. It is unclear from the analysis how the sample populations in Bins I, II, and III compare on these characteristics. For example, if the Bin III (and more importantly, its subgroups) population has a larger Body Mass Index (BMI) than the average US population, the sample population may consume more food than average. In this scenario, Bin III's absolute amount of perchlorate may be larger than the typical person in the US.

* Sample Population Size. The importance of describing the sample in more detail is magnified by the small number of individuals in the sample results EPA uses. EPA uses the 90th percentile result from the 98 pregnant women in Bin III. EPA has not described the statistical relation of this sample to the US population. In addition, based on the shape of the distribution described in Blount (2006), the upper percentile results must be driven by relatively few observations. In other words, the analysis relies on the results from just a few women of unknown relationship to the whole US population or the subpopulation of pregnant women.

Viewed in this way, EPA's analysis is a convenience, non-statistically representative sample that is comparable to other study populations in Greer et al. (2002), Pearce et al. (2007), Tellez et al. (2005), and Amati et al. (2007). These studies all show that for total doses in excess of the RfD, there are no measurable adverse health effects on the study populations, including sensitive populations. Therefore, while EPA constructs this study population to estimate an RSC, it primarily reinforces the PSG's position that no effects occur below the RfD even for sensitive subpopulations. Until EPA provides more description of its study population, its advantages over the other published, peerreviewed studies is unclear.

* Temporal Comparison. In its background document, EPA describes how it linked the two study populations in the dimension of space - EPA assigned individuals to the bins based on whether a drinking water system in the county reported any single detection of perchlorate. EPA notes, but does not fully describe, how EPA handled temporal associations. The UCMR data was gathered from 2000 to 2005 according to EPA. The NHANES survey was conducted during 2001 and 2002. It is not clear whether EPA only used the UCMR counties that reported detections in 2001 and 2002 or all years in the UCMR dataset. This consideration is important since many systems that detected perchlorate did not do so routinely. If EPA used the UCMR data from all years, EPA should describe how many individuals in the Bin III subgroups lived in counties with an actual detection during the 2001-2002 time period.

Additionally, on the NHANES sample, it is unclear how EPA adjusted the food consumption data to reflect seasonality. People eat different foods at different times of the year. While NHANES adjusts for this fact in its study design, it is unclear how and if EPA did so in its subsample. For example, if 50 percent of the pregnant women in Bin III were surveyed by NHANES in the summer, the food consumption patterns (and the distribution of absolute levels of perchlorate) would be different than if only 25 percent were sampled during that time.

* Concentrations below Detection Limits Assumed to be Zero. EPA notes that one limitation is that the analysis assumes that all detections below 4 ppb are assumed to zero. EPA states:

It is uncertain how the 4 ug/l detection limit in the UCMR might affect the assignment of NHANES to Bin III. However, EPA believes that the classification is reasonable and that it is unlikely that any false negatives would significantly change the findings because there is a low frequency of occurrence above the method reporting limit (less than two percent of all samples had detects), it is reasonable to assume that there would be a corresponding low frequency of occurrence below it if at all. (EPA envisions a scenario with a high frequency of occurrence at very low concentrations unlikely). (pg 13)

First, while the misclassification problem among bins is interesting, it is clear how the detection limit will bias the results within Bin III. Bin III is supposed to represent individuals that only receive

perchlorate through food. EPA uses the Bin III results to calculate the dose received from food. If some of this dose actually derives from drinking water, EPA is overestimating the dose from food, underestimating allowance available from drinking water, and underestimating the HRL.

Consider this scenario. In the pregnant women subgroup of Bin III, the 98 pregnant women have an average estimated perchlorate intake of 0.123 ug/kg/day. In the analysis, EPA assumes the water contribution is zero. Suppose the true water concentration for the 98 women is 1/2 the detection limit (or 2 ug/l), a common EPA assumption in risk assessments and other 13 drinking water exposure scenarios. The women then receive a dose of 0.057 ug/kg/day from drinking water. This amount is 46 percent of their total dose. Their estimated food dose is correspondingly lower, the relative source contribution would be lower, and the HCL should be greater than 15 ppb. While the 1/2 the detection limit is merely an assumption, it illustrates the main point - the censoring of the data due to the detection limit can have a large effect on the Bin III results.

This effect will only be large if a significant proportion of the Bin III population has concentrations of perchlorate in drinking water below the levels of detection. EPA finds "high frequency of occurrence at very low concentrations unlikely." If "high" means 90 percent of the population, this scenario is unlikely.

Table 2 in the proposed determination shows the estimated population served with at least one sample above the detection limit has an exponential shape to it (each time the concentration is cut in half, the estimated population exposed at that level doubles.) It is reasonable to assume that this relationship continues below the detection limit. By assuming all people in Bin III receive no perchlorate from drinking water, EPA overestimates the concentration from food and creates an overly conservative HRL.

In summary, EPA's approach is scientifically appropriate in using actual observed data to estimate the RSC and the HCL. All approaches have limitations; however, any limitations in EPA's analysis have to be viewed in context of the extensive body of literature on perchlorate's mode of action and measured effects in humans. When EPA's analysis is viewed in the context of the NAS findings and other published studies, EPA's analysis is one more way to demonstrate that total exposure to perchlorate in the US is common and without adverse effect. EPA's analysis is more than adequate to demonstrate that perchlorate does not occur at a frequency and level of health concern to warrant an NPDWR.

Response: See response to comment code 5220 for a discussion of the alternative Health Reference levels. Your observations regarding some limitations of the Huber et al. study are correct, and as you note changes in dietary habits or food sources over a year or the possibility of small water contribution to what is considered food-only source would change results in a minor way. Because NHANES collects samples at different times of the year the result we obtained will be applicable for the entire year, and small changes would not be significant from a health standpoint. The gap in the data of course is the lack of information on children less than 6 years old which has become a focus of concern.

Commenter Name: Ellen Blaschinski, M.B.A., R.S.
Commenter Organization: Regulatory Services Branch, Connecticut Department of Public Health
EPA Document ID: EPA-HQ-OW-2008-0692-2091
EPA Comment ID: 21115

EPA Comment Code: 5220

Comment: However, in the October 10th Preliminary Regulatory Determination, EPA decided not to set a federal MCL for perchlorate. This was based upon the establishment of a drinking water Health Risk Limit (HRL) of 15 ug/L as the bright line for evaluating how many people would be exposed to concentrations of concern. The numerical target of 15 ug/L can be questioned on a number of fronts given that other recent derivations by states governments have yielded drinking water targets of 2 to 6 ug/L (New,Jersey, Massachusetts, California). The EPA assessment supporting the 15 ug/L HRL was reasonable in some regards (e.g., the mannner in which the relative source contribution was derived) but is not well justified when it comes to the level of exposure allowed for breast and bottle- fed infants. EPA's own assessment puts this early life exposure at 2 to 5 times greater than the Agency's RfD, with this justified by the use of an exploratory pharmacokinetic model which has no possibility of being validated for children. Given that this a key population to protect, it is essential that the HRL be set such that the RfD is not exceeded in this group. This is especially the case given that the health protectiveness of the RfD has been questioned by the CDC study, which shows quite clearly that effects on thyroid hormone status are possible at levels of perchloratc below the RfD in adult women (Blount et al. 2006).

The establishment of a lower HRL, more in line with recent derivations within several states, would yield a considerably larger public health impact than what was put forth by EPA in its draft determination. Therefore, this needs to be carefully reassessed. Our recommendation for a reassessment is in line with EPA's own Science Advisory Board which called EPA's decision premature stating that; "Given perchlorate's wide occurrence and well-documented toxicity to humans, the Science Advisory Board strongly believes that there must be a compelling scientific basis to support a scientific determination not to regulate perchlorate as a national drinking water contaminant" (SAB letter, November 5, 2008).

Response: See response to comment code 5220.

Commenter Name: Mark S. Mayer
Commenter Organization: South Dakota Department of Environment & Natural Resources (DENR)
EPA Document ID: EPA-HQ-OW-2009-0297-0467
EPA Comment ID: 28482
EPA Comment Code: 5220

Comment: - Comment on the Health Reference Level Issues - South Dakota DENR agrees the process presented appears to be reasonable.

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Richard Nieuwenhuis
Commenter Organization: New Jersey Farm Bureau (NJFB)
EPA Document ID: EPA-HQ-OW-2009-0297-0665
EPA Comment ID: 28534
EPA Comment Code: 5220

Comment: Moreover, the Environmental Protection Agency has not presented any sound scientific evidence that sufficiently explains why the previous health reference level (HRL) that supports a drinking water equivalent of 15 ug/L is inadequate. The 15 ug/L HRL was established from scientifically supported literature and based on the most sensitive sub-population, plus an added ten-fold safety factor.

We understand that the scientific evaluation of perchlorate has become complicated over the past few years but believe that there remains a significant need for more comprehensive scientific evaluation and debate.

We appreciate your attention to our concerns.

Sincerely, Richard Nieuwenhuis President

Response: See response to comment ID 28799 under comment code 5220.

Commenter Name: Anthony Russo
Commenter Organization: Chemistry Council of New Jersey (CCNJ)
EPA Document ID: EPA-HQ-OW-2009-0297-0673
EPA Comment ID: 28688
EPA Comment Code: 5220

Comment: October 6, 2009

Water Docket Environmental Protection Agency Mailcode 2822T 1200 Pennsylvania Avenue Washington, DC 20460

RE: "Drinking Water: Perchlorate Supplemental Request for Comments" 74FR159:41883, August 19, 2009

Dear Sir/Madam:

The Chemistry Council of New Jersey (CCNJ) represents the interests of over 100 manufacturers in the business of chemistry in the Garden State. Our mission is to advance members' interests, operational and environmental excellence, science education and community outreach.

The CCNJ appreciates this opportunity to provide comments on the above referenced public notice regarding alternative approaches to the interpretation of scientific data relevant to a regulatory determination for perchlorate in drinking water.

CCNJ has several concerns about this issue. We believe that good public policy must be developed and proposed using sound, proven scientific data and presented in a manner which the public can understand and make informed judgments to determine application and appropriate risk prevention practices.

Repeated scientific investigation, including a landmark National Academy of Sciences (NAS) review, result in a clear and consistent conclusion: low levels of perchlorate are not dangerous to public health. We should not ignore this data. Without the presentation of supporting scientific literature

justifying alternative analysis, it becomes difficult for EPA to demonstrate why this alternative would support a science based regulatory determination under the Safe Drinking Water Act (SDWA). Not only has EPA not presented any justification for an analysis based on an alternative health reference level that uses water intake and body weight measurements at specific life stages, but EPA has also not presented any scientific evidence that indicates why the previous HRL that supports a drinking water equivalent of 15 ppb, based on the most sensitive subpopulation, with an added ten fold safety factor and derived from the scientifically supported literature is inadequate.

Response: See response to comment ID 28799 under comment code 5220.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28799
EPA Comment Code: 5220

Comment: EPA tried to support its conclusions that a 15 ppb HRL is safe by avoiding reference to the RfD, and instead referring to the level of inhibition of radioactive iodide uptake (RAIU) on which the NRC report (NRC, 2005) based its recommended RfD.[FN32: 73 Fed. Reg. at 60277.] EPA cannot shift its evaluation of acceptable exposure estimates to a discrete biological endpoint that leads to exceedances of the RfD.

Response: In the October 2008 preliminary regulatory determination, EPA had derived a single HRL of 15 µg/L based upon the RfD, an estimate of perchlorate exposure from food for pregnant women, and traditional adult body weight (70 kg) and drinking water consumption (2 L/day) values. This single HRL was derived to reflect exposure to a pregnant woman and her fetus, which the NRC identified as "the most sensitive population."
Since the NRC also identified infants and developing children as additional life stages, EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 µg/L to 47 µg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These HRLs are calculated based on individuals who consume an average amount of perchlorate from food (except for pregnant women where EPA used a 90th percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts. EPA has developed potential health reference levels (HRLs) for perchlorate for purposes of this regulatory determination. HRLs are not final determinations about the level of a contaminant in drinking water that is necessary to protect any particular population. Rather they are benchmarks against which EPA compares the concentration of a contaminant found in public water systems to determine if it is at levels of public health concern.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28802
EPA Comment Code: 5220

Comment: RESPONSE TO REQUEST FOR COMMENTS ON THE HRL

In simple terms, the HRL is the maximum tolerable amount of perchlorate that could be in drinking water, considering that perchlorate is also in food, and still keep daily consumption levels from exceeding the RfD. The 2008 proposed HRL of 15 ppb was calculated as follows: For all populations, including pregnant women, EPA determined that the RfD is 0.7 ug/kg/day. This value is posted on the IRIS database based on recommendations from a committee of the NRC. EPA reports that for pregnant women, exposure to perchlorate from food is 0.263 ug/kg/day at the 90th percentile (based on data from a national food survey), representing nearly 38% of the RfD, thus leaving an relative source contribution (RSC) for water of 62%.[FN43: 73 Fed. Reg. at 60276)] This is equivalent to 0.437 ug/kg/day from water, assuming an average body weight of 70 kg, and a daily water consumption of 2 L (90th percentile adult water consumption). That is, 0.437 ug x 70 kg body wt. = 30.6 ug perchlorate in 2 L (the daily consumption amount). This is 15 ug/L, or 15 ppb, the HRL proposed in the October 2008 FR notice.

Response: No response necessary to this summary of EPA information.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Department of Environmental Protection (NJDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0527
EPA Comment ID: 28916
EPA Comment Code: 5220

Comment: Based on the above comments, we urge USEPA to reconsider its proposed HRL of 15 ug/L.

Response: See response to comment ID 28799 under comment code 5220.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 29096
EPA Comment Code: 5220

Comment: Because the RfD was based exclusively on the dose-response calculations derived from the Greer et al study, then the HRL also relies on that data to derive a maximum allowable level of drinking water contamination. The derivation of a health-based standard for perchlorate should reflect the best available data, including published data collected and analyzed by the CDC and described by Blount (2006) and Blount (2007).[FN43: Blount BC, Valentin-Blasini L, Osterloh JD, Mauldin JP, Pirkle JL. Perchlorate exposure of the US Population, 2001-2002. J Expo Sci Environ Epidemiol. 2007 Jul;17(4):400-7. Epub 2006 Oct 18. Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environ Health Perspect. 2006 Dec;114(12):1865-71.] As noted above, these data have the following advantages over the Greer et al data:

1. Although the CDC data are from a cross-sectional analysis, because the survey includes a large number of individuals, the variability represents random error, not bias, and the data are likely to be representative of chronic perchlorate exposure;

2. The number of individuals included in the CDC study are sufficient for the specific analysis of a sensitive subpopulation defined as women with low iodine intake;

3. A benchmark dose (BMD) analysis of perchlorate-related modulation of serum thyroid hormone concentrations is feasible; and

4. Perchlorate exposures, as measured by urinary perchlorate concentration, corresponding to the benchmark dose low (BMDL) can be converted to an estimated dose in mg/kg-day, that can be used as the point of departure for the derivation of both the MCL and HRL.

The mean for total serum T4 concentrations in women is 8.27 ug/dL and the 25th percentile of perchlorate exposure (equivalent to 1.6 ppb perchlorate in urine) is associated with a 10% drop in total serum T4 in women with low iodine intake.[FN44: Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environ Health Perspect. 2006 Dec;114(12):1865-71.]

Response: See response to comment ID 28863 under comment code 2110.

EPA Comment Code: 5225 Use of alternative HRLs specific to sensitive life stages, as described in Table 2 of the August 2009 FR notice.

Individual Comments
Commenter Name: W. Cucinotta
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0038
EPA Comment ID: 28338
EPA Comment Code: 5225

Comment: Enclosed are my comments on your approaches for deriving HRLs on Perchlorates and other chemicals in our drinking water.

4.

a. No, I do not feel EPA appropriately took into account specific and appropriate exposure values for all potentially sensitive life stages, including infants, children and the fetuses of pregnant women. Any exposure to these type of chemicals should be eliminated and controlled to protect Americas' drinking waters. The 70 kg body weight and 2 liter per day consumption used for past regulatory determinations are grossly inappropriate levels to consider safe.

b. I feel none of these these values are low enough to be appropriate levels to determine health concerns against which to compare the levels of perchlorates found in public water systems. I urge you to adopt the smallest exposer levels considered or preferably lower them to no (0) exposure at all.

c. I feel the EPA did not use the best available and most appropriate data to estimate alternative HRLs in Table 2 because you cannot control how much water any one person consumes or the amount of perchlorate exposure from other sources. No, your drinking water ingestion rates in Table 2 do not take into account the life stages (birth to 6 months, and women ages 15-44) and does not provide an accurate representation of the exposure to the most vulnerable life stages because you cannot control how much water any one person consumes or the amount of perchlorate exposure from other sources.?

Response: See response to comment code 5220 for a discussion of the HRLs. Regarding health implications of exposures above the HRLs, the data underlying the definition of iodide uptake inhibition as a precursor effect and the relationship of iodide uptake inhibition to the continuum of adverse outcomes reflects an understanding of effects in adults; it may not reflect the relationship of the precursor event to adverse outcomes in children. We know that thyroid hormone status in neonates and infants is less resilient than in adults. That is, in general, neonates and infants may not have iodide stores sufficient to offset the effects of reduced iodide uptake. Half-lives for circulating hormones in neonates and infants are shorter than for adults, making neonates and infants less able to maintain stable hormone levels in the face of a chemical insult. The less resilient neonatal and infant system makes the exposure gap between a precursor event (iodide uptake inhibition due to perchlorate) and reduced T3/T4 levels likely to be narrower than for adults, and in fact, the distinction between the two may be blurred for the very young (Greer et al., 2002; Savin et al., 2003; van den Hove et al., 1999). The NRC noted that, "[T]he minimal prolonged decrease in thyroid

hormone production that would be associated with adverse health effects is not known; any decrease is potentially more likely to have adverse effects in sensitive populations (people with thyroid disorders, pregnant women, fetuses, and infants) but data are not available to determine the magnitude of the decrease needed to cause adverse effects in those populations." The additional sensitivity of these groups to perturbations in thyroid hormone levels, and the uncertainty about the point in the continuum of effects at which adverse effects occur are important considerations in concluding that perchlorate exposures above the RfD are likely to have an adverse effect on the health of sensitive life stages. Therefore, we do not agree with those commenters who stated that levels of perchlorate in drinking water that result in exposures greater than the RfD are not levels of public health concern.

Commenter Name: James D. Taft
Commenter Organization: Association of State Drinking Water Administrators
EPA Document ID: EPA-HQ-OW-2009-0297-0525
EPA Comment ID: 28498
EPA Comment Code: 5225

Comment: Comments on the Health Reference Level (HRL) Issues - While we are generally comfortable with the development of the alternative HRLs in Table 2 (page 41888), the key question is: what HRL should be used as the basis of the regulatory determination? This is where we have some concern. Ideally, the regulation of a contaminant would be targeted at the most sensitive subpopulations, no matter how small the subpopulation. However, we must also be cognizant of resource limitations and practical constraints. It may not be feasible to protect very small subpopulations with a general regulation but rather, it may be more appropriate to use other risk reduction approaches to target small groups that may have special sensitivity. We cannot recommend a specific HRL without a full understanding of the implications on the burden for water systems and states, which these data do not provide. The HRL of 15 ug/l, derived using the traditional approach, is a good starting point and would cover a large percentage of the population. In addition, EPA should evaluate a range of HRLs between 15 and 4 ug/l in connection with more sensitive subpopulations. The Agency could then consider these values, in combination with occurrence data, in order to determine the populations that could be protected by regulation and whether regulation at these lower levels would present a "meaningful opportunity for health risk reduction", as required by the Safe Drinking Water Act.

Response: See response to comment code 5220.

Commenter Name: Shannon Cunniff
Commenter Organization: Department of Defense (DOD)
EPA Document ID: EPA-HQ-OW-2009-0297-0411
EPA Comment ID: 28518
EPA Comment Code: 5225

Comment: Department of Defense Comments on the August 19, 2009 USEPA Federal Register Notice [EPA-HQ-OW-2009-0297; FRL-8943-9] Drinking Water: Perchlorate Supplemental Request for Comments Pages 41883-41893

Comments submitted by: Chemical Material Risk Management Directorate Organization: Department of Defense Date Submitted: 18 September 2009

*Comment categories: Science or methods (S); Editorial, grammar/spelling, clarifications needed (E); or Other (O). Also please indicate if Major (M), i.e. affects the outcome, conclusions or implementation of the assessment.

Comment No. 1

Section

Page & Paragraph Global

Comment As noted in his 9 March 2009 memorandum on Scientific Integrity, President Obama recognizes that science and the scientific process must inform and guide Administration decisions on a wide range of issues, including improvement of public health, protection of the environment. The memo underscores the importance of scientific integrity by further noting that if the public is to trust the science and scientific process informing public policy decisions there should be transparency in the preparation, identification, and use of scientific and technological information in policymaking. In embracing the President's commitment to scientific integrity, Administrator Jackson notes in her 9 May 2009 memorandum to EPA employees that the Agency's regulatory decisions should include a full explanation of the science issues addressed by the Agency, the data relevant to those issues, and the interpretations and judgments underlying the Agency's scientific findings and conclusions.

Suggested Action, Revision and References (if necessary) To ensure consistency with Administration and Agency commitments to scientific integrity, the following issues need to be considered in a transparent and scientifically defensible manner prior to the determination of any Health Reference Level (HRL), because they can impact the conclusions drawn by the EPA in the potential for health risk reduction for perchlorate in drinking water. While these issues do not address all requests for comments on alternative approaches, they focus on issues that will have the most significant impact on the determination and acceptance of an alternative HRL. The main issues associated with the alternative approaches presented by EPA (2009) include the following: 1. The lack of transparency and assurance of quality in the determination of alternative HRLs. 2. Inadequate characterization of exposure to sensitive subgroups, specifically infants and the fetuses of pregnant women. 3. A lack of justification for elimination of the PBPK models from consideration in the determination of an HRL. 4. Recommended applications for the PBPK models in the development of an HRL.

Category* S, M

Response: EPA believes that it has been consistent with Administration and Agency commitments to scientific integrity. The August 2009 notice clearly discusses the basis for alternative health reference approaches and that EPA was re-evaluating how best to incorporate PBPK modeling analysis into its evaluation of perchlorate, if at all.

Commenter Name: Shannon Cunniff
Commenter Organization: Department of Defense (DOD)
EPA Document ID: EPA-HQ-OW-2009-0297-0411
EPA Comment ID: 28519
EPA Comment Code: 5225

Comment: Comment No. 2

Section

Page & Paragraph Global

Comment The current documentation of the suggested alternative HRLs based on body weight and water consumption of other life stages is inadequate. The development of this alternative approach relies heavily on the FDA total dietary survey (Murray et al. 2008) and the first Unregulated Contaminant Monitoring Regulation (UCMR 1). While these studies are well conducted and provide a significant resource for information, the documentation provided is not sufficient to demonstrate their application, nor to insure their reproducibility by other parties.

Suggested Action, Revision and References (if necessary) To insure clarity it is recommended that sufficient documentation be provided. Under the Data Quality Act (Section 515 of the Treasury and General Government Appropriations Act of 2001 (PL 106-544, H.R. 5658), Federal agencies are charged with ensuring the quality, integrity, and objectivity of information provided. See also comment #s 11 and 14.

Category* E, M

Response: EPA disagrees that the documentation of the suggested alternative HRLs is inadequate. In the October 2008 and August 2009 notices, EPA presents in detail the Unregulated Contaminant Monitoring Rule data as well as the Food and Drug Administration's Total Diet Study in 73 FR 60269–72. EPA has described how those studies have been used in deriving health references. EPA believes these are the best available peer reviewed data and that they have been applied in a reproducible manner.

Commenter Name: Shannon Cunniff
Commenter Organization: Department of Defense (DOD)
EPA Document ID: EPA-HQ-OW-2009-0297-0411
EPA Comment ID: 28520
EPA Comment Code: 5225

Comment: Comment No. 3

Section

Page & Paragraph Global

Comment By removing the PBPK models from consideration, the agency has effectively removed consideration of the age-dependent variations in biology, and is apparently assuming that all differences may be accounted for by addressing the differences in exposure. There are many age-dependent differences, including exposure, clearance, protein binding, and NIS capacity, as well as extrathyroidal sites of iodide inhibition (placenta, milk) that influence perchlorate toxicology. The models were developed using specific data to quantify these differences, and while uncertainty may exist in specific parameter values, it is certainly better to estimate parameter values from data rather

than ignoring their existence. Factors such as clearance, maternal-fetal transfer, and extrathyroidal inhibition cannot be addressed in a standard analysis based on adjusting Points of Departure (PoDs) by exposure differences. Indeed, in the current proposal, the uncertainty associated with these parameters is added to other uncharacterized uncertainty, which does not improve estimates of risk.

The alternative HRL approach represents, in fact, a decision to become less informed about the processes governing potential increased risk to the sensitive populations, giving the impression that it is better to ignore the uncertainty related to real biology than to attempt to account for it.

Suggested Action, Revision and References (if necessary) Instead of using the 90th percentile for exposure and an RSC, a more mathematical approach should be used to assess uncertainty in model predictions (i.e., Monte Carlo). This would help define expected ranges of inhibition after taking into account both variability in exposure and intraspecies variability in biological parameters. Not only would this be a more quantitative way of accounting for uncertainty in exposure, but it would also address commenter's concerns about the model parameter uncertainty and transparency.

Category* S. M

Response: EPA disagrees that by not using the PBPK model the Agency is deciding to become less informed. See response to comment ID 20432 under comment code 5220 for a discussion of EPAs decision not to utilize the PBPK model.

Commenter Name: Shannon Cunniff
Commenter Organization: Department of Defense (DOD)
EPA Document ID: EPA-HQ-OW-2009-0297-0411
EPA Comment ID: 28523
EPA Comment Code: 5225

Comment: Comment No. 11

Section III. B. 3. Alternative Approaches for Calculating HRLs

Page & Paragraph Page 41888 Column 1 Para 1

Comment Example of comment # 2: The document relies on information to characterize ingestion to early life stages, which represent a sensitive subgroup, based on sample sizes that do not meet minimum data requirements. While EPA (2009) states that these are the best available data, there is no indication that a comprehensive literature search was conducted to determine if additional data could be used to supplement or validate the data provided.

Suggested Action, Revision and References (if necessary) It is recommended that a comprehensive literature search be performed and documented.

Category* E

Comment No. 12

Section III. B. 3. Alternative Approaches for Calculating HRLs

Page & Paragraph pg 41888 Column 1-3

Comment Based on the EPA's analysis of percent radioactive iodide uptake (RAIU) inhibition estimated with the PBPK model (Table 8, EPA 2008), the NRC (2005) identified the 7-day old breast-fed infant and the fetus of the pregnant woman at 40 weeks as the most sensitive subgroups. Yet, in their attempt to develop alternative HRLs based upon body weight and water consumption, which appears to be the only alternative presented, EPA (2009) has not adequately characterized exposure to perchlorate by these subgroups. The Relative Source Contribution for perchlorate from food for the birth to 12 month life stages (Table 2, EPA 2009) is based on information provided in the FDA Total Dietary Survey (Murray et al. 2008). The EPA (2009) states that because no information was available from the TDS for the life stages from birth to 6 months of age, estimates for the nearest age range (6-12 months) was used. The intake from food provided by Murray et al. (2008) largely results from the determination of perchlorate in baby food and commercial formula ingested by children aged 6-11 months. From birth to six months, however, baby food would not be a significant portion of the diet. If intake is assumed to be mainly from commercial formula, the RSC may be similar, but this is a major uncertainty. Furthermore, intake from breast milk is not addressed at all using the HRL approach. It is not reasonable to assume the same dietary ingestion in the newborn ingesting breast milk alone, and the child that is eating solid food. It is, in fact, impossible to define perchlorate exposure in the breast-fed infant or the fetus, using this revised approach for defining an HRL.

Suggested Action, Revision and References (if necessary) It is recommended that the alternative HRLs not be used to estimate risk for this sensitive subgroup.

Environmental Protection Agency (EPA). 2008. Drinking Water: Preliminary Regulatory Determination on Perchlorate. Federal Register 73(198):60262-60282.

National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology. January, 2005.

Category* S. M

Response: Regarding the recommendation to conduct and document a comprehensive literature search on information to characterize ingestion to early life stages, EPA believes that it did just that in developing EPA's "Child-Specific Exposure Factors Handbook." The information in the Handbook represents the best available peer reviewed data on drinking water ingestion rates for various life stages.

Regarding the recommendation that alternative HRLs not be used to estimate risks for sensitive groups, EPA strongly disagrees. The NRC (2005) identified fetuses of iodide deficient pregnant women are the most sensitive life stage and also identified infants and developing children as sensitive life stages. . EPA estimates that at least 5.1 to 16.6 million people are served by PWSs, for which we have data, that have perchlorate contamination.

EPA has determined that a NPDWR for perchlorate may reduce perchlorate exposures for these infants, children, and pregnant women to levels below the RfD, and therefore believes that this

perchlorate exposure reduction presents a meaningful opportunity for the reduction of health risks for persons served by PWSs.

EPA has made this determination based on a consideration of the best available peer reviewed science and data collected in accordance with accepted methods related to perchlorate occurrence in drinking water, the presence of perchlorate in foods, and the health effects of exposure to perchlorate.
National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276pp.

Commenter Name: Shannon Cunniff
Commenter Organization: Department of Defense (DOD)
EPA Document ID: EPA-HQ-OW-2009-0297-0411
EPA Comment ID: 28524
EPA Comment Code: 5225

Comment: Comment No. 13

Section III. B. 3. Alternative Approaches for Calculating HRLs

Page & Paragraph Page 41888 Column 1-3

Comment The major problem with the current approach is the lack of characterization of exposure by those sensitive subgroups identified by NRC (2005): the 7-day old breast fed infant and the fetus of the pregnant woman at 40 weeks of gestation. The available dietary surveys and drinking water ingestion rates are incapable of providing a means to determine potential intake for these sensitive subgroups.

Suggested Action, Revision and References (if necessary) Incorporation of a PBPK model at this step would provide a reasonable method for estimating maternal transfer of perchlorate. One of the major strengths of the PBPK models is that they provide a platform for estimating fetal and infant dose using biological data on transfer rates and pharmacokinetic data in both the animal and human. These models have been tested against human iodide data, and when available, perchlorate data. It is true that the data sets available for validation were extremely limited. However, even limited data are better than the complete lack of data available to support the new approach. Derivation of an HRL for the breast fed infant and fetus needs to consider such complex biological processes as placental transfer, active uptake in the mammary gland, and extrathyroidal inhibition. In 2008, the PBPK models were used to address these issues. The current approach does not utilize the PBPK models, and in the process does not consider what is known about the important biological determinants of perchlorate transfer to the fetus and infant, the identified sensitive subgroups.

Category* S. M

Response: See response to comment ID 20432 under comment code 5220.

Commenter Name: Shannon Cunniff
Commenter Organization: Department of Defense (DOD)

EPA Document ID: EPA-HQ-OW-2009-0297-0411
EPA Comment ID: 28526
EPA Comment Code: 5225

Comment: Comment No. 15

Section IV. Consideration of Studies Published Since EPA Adopted the NAS RfD for Perchlorate

Page & Paragraph Pages 41889 41891

Comment EPA requests comment on whether EPA used the best available and most appropriate data to estimate alternative HRLs in Table 2.

The HRL it is too simplistic and does not take into account the full range of scientific knowledge regarding coexposure to chemicals known to also bind to the NIS receptor. For example, it does not allow taking into account other relevant issues concerning thiocyanate and nitrate co-exposures. It also does not consider factors such as potential differences in the perchlorate "half-life" compared to thiocyanate and nitrate, and comparison of thyroid hormone effects.

Suggested Action, Revision and References (if necessary) Evaluate the above referenced (see Comment #10) human sensitive subpopulation data using direct measurement of biological fluids to derive the HRL for perchlorate considering the cumulative risk of other goitrogens (thyocianate and nitrate from dietary sources). These data should be considered for use in and/or validation of the EPA models.

Since not just perchlorate but also thiocyanate and nitrate are present in commonly ingested foods, as well as mother's and bovine milk, they all impact iodide uptake inhibition, and thus should be evaluated

Category* S

Response: While EPA acknowledges that nitrate and thiocyanate have the same mode of action as perchlorate, and that the effects of combined exposure to perchlorate, nitrate, and thiocyanate are additive, EPA does not believe there are sufficient scientific data currently available to assess and characterize the combined risk of these contaminants. EPA has committed to a drinking water strategy that outlines four principles to expand public health protection for drinking water (USEPA, 2010b). One of these principles is to address contaminants as groups. However, EPA does not believe that regulatory action to address perchlorate should be further delayed. Therefore, EPA intends to develop a proposed rule for perchlorate. At such time as a NPDWR is promulgated, EPA is required to review and revise, as appropriate, its drinking water standards at least every six years. Any revision must at least maintain or improve public health protection. When there are sufficient scientific data to assess the cumulative risks of perchlorate and other contaminants, EPA will review this information to evaluate whether any revisions of NPDWRs are appropriate.

Commenter Name: Kathy Dolan
Commenter Organization: Food and Water Watch (FWW)
EPA Document ID: EPA-HQ-OW-2009-0297-0526
EPA Comment ID: 28610

EPA Comment Code: 5225

Comment: As suggested by previous commenter's, I believe that the Agency's proposed HRL, of 15 micrograms/Liter, is too high. The alternative HRLs presented in Table 2 of your request for comment notice, dated August 5, 2009, do not use the most appropriate data. The data in Table 2 uses mean ingestion rates from the CSFII. The CSFII is already several years out of date.

Response: See response to comment code 5220. Regarding use of CSFII data, EPA believes that it is the best peer reviewed science that is available on the consumption of drinking water.

Commenter Name: Apparent Mass Mailing #11 - Food and Water Watch
EPA Document ID: EPA-HQ-OW-2009-0297-0526
EPA Comment ID: 28616
EPA Comment Code: 5225

Comment: As suggested by previous commenter's, I believe that the Agency's proposed HRL, of 15 micrograms/Liter, is too high. The alternative HRLs presented in Table 2 of your request for comment notice, dated August 5, 2009, do not use the most appropriate data. The data in Table 2 uses mean ingestion rates from the CSFII. The CSFII is already several years out of date.

Response: Regarding the Agency's proposed HRL of 15 ug/L being too high, see response to comment code 5220. Regarding use of CSFII data, EPA believes that it is the best peer reviewed science that is available.

Commenter Name: Sonia Salas
Commenter Organization: Western Growers Association on behalf of several California agriculture groups
EPA Document ID: EPA-HQ-OW-2009-0297-0652
EPA Comment ID: 28676
EPA Comment Code: 5225

Comment: The California agriculture groups submitting this letter appreciate the opportunity to comment on USEPA's August 19, 2009, Federal Register notice seeking comment on "additional approaches available for analyzing data related to EPA's perchlorate regulatory determination. The attached letter contains specific comments and information. Thank you for your consideration.

October 8, 2009

Mr. Eric Burneson Office of Ground Water and Drinking Water Standards and Risk Management Division Environmental Protection Agency 1200 Pennsylvania Avenue, NW Washington, DC 20460

Subject: California Agriculture Industry Comments on Docket Identification (ID) EPA-HQ-OW-2008-0692-Perchlorate Supplemental Request for Comments

Dear Mr. Burneson:

The undersigned California agriculture groups appreciate the opportunity to comment on USEPA's August 19, 2009, Federal Register notice seeking comment on "additional approaches available for analyzing data related to EPA's perchlorate regulatory determination." Since a national primary drinking water standard for perchlorate would directly impact public perception of the safety of agricultural commodities known to contain trace amounts of perchlorate, it is critical that EPA establish the appropriate science-based methodology before proceeding with a final regulatory determination.

The California agriculture industry is a $37 billion industry that produces more than 350 different crop and livestock commodities and generates an estimated $100 billion in related economic activity. California agriculture accounts for approximately 7.5% of all employment and supports more than a million on-farm jobs. California agriculture is also the leading global exporter of agricultural commodities, sending almost 20% of our agricultural production to foreign markets.

EPA's Proposed Alternative Health Reference Levels are Not Scientifically Justified and will Undermine Public Confidence in the Safety of Agricultural Commodities.

EPA's August 19, 2009, Federal Register notice states that the "additional alternatives under consideration could result in health reference levels which are much lower than the level identified in the October 2008 notice." This statement causes great concern for the California agriculture industry because it implies that exposure to trace amounts of perchlorate may be harmful to human health, when in fact, the rich body of scientific literature on perchlorate does not support this conclusion. It is well established that many agricultural commodities contain trace amounts of perchlorate, but these levels are widely recognized as being orders of magnitude below any level that may pose a risk of adverse human health effects. EPA's promotion of the alternative health reference level concept will needlessly rekindle public concern about the safety of agricultural commodities and will drive some consumers away from these products to avoid perchlorate exposure. The negative impacts on public health associated with such a shift in dietary habits will vastly outweigh the risk of harm associated with exposure to trace amounts of perchlorate.

Response: We appreciate your concern that food not be negatively impacted by evaluations of perchlorate in drinking water. The drinking water regulatory determinations health reference levels (HRLs) are calculated for public tap water and consider how much of the RfD is already taken by food exposure using a relative source contribution (see response to comment code 5220). Drinking water with perchlorate at levels less than the HRL may prevent the water-plus-food components of exposure from exceeding the RfD.

Commenter Name: Anthony Russo
Commenter Organization: Chemistry Council of New Jersey (CCNJ)
EPA Document ID: EPA-HQ-OW-2009-0297-0673
EPA Comment ID: 28690
EPA Comment Code: 5225

Comment: The Agency has sufficient data to show that perchlorate will not have an adverse effect on the health of persons at the levels expected in public drinking water systems, having based its RfD on a no observed effect level (NOEL) of a precursor to an adverse effect. Based on the available data, neither the first nor the second criteria of the SDWA are met.

EPA along with other experts including the NRC committee, ATSDR and OEHHA have all identified the most sensitive life stage as the fetuses of hypothyroid or iodine deficient pregnant women. The NRC committee determined that all sensitive subpopulations, including infants, would be protected by the drinking water equivalent of EPA's reference dose, 15 parts per billion (ppb). By proposing to base its calculation of alternative health reference levels (HRL) on specific life stages as opposed to the calculation based on the most sensitive sub- population (fetus), EPA would establish a scientifically unsupportable precedent that could then be applied to every other water contaminant for which and MCL has been established. EPA's calculation of alternative health reference levels (HRL) is not the best available science and thus runs contrary to EPA's duty under the Safe Water Drinking Act.

Response: See response to comment ID 28338 under comment code 5225.

Commenter Name: Kay Brothers
Commenter Organization: Southern Nevada Water Authority
EPA Document ID: EPA-HQ-OW-2009-0297-0667
EPA Comment ID: 28697
EPA Comment Code: 5225

Comment: Alternative Health Reference Levels (HRLs) Based Upon Body Weight and Water Consumption of Other Life Stages

Studies have clearly proven that perchlorate is a naturally occurring chemical which is absolutely ubiquitous in the environment (Sanchez, Krieger et al. 2005; Snyder, Vanderford et al. 2005; Valentin-Blasini, Mauldin et al. 2005; Baier- Anderson, Blount et al. 2006; Blount, Pirkle et al. 2006; Blount, Valentin- Blasini et al. 2006; Snyder, Pleus et al. 2006; Dyke, Ito et al. 2007). The evidence of perchlorate's ubiquity is indisputable based on the recent NHANES and FDA Diet Study, which clearly demonstrated that perchlorate is present in the human diet; thus, increasing the challenge of demonstrating "a meaningful opportunity for health risk reduction for persons served by public water systems" through federal regulation of perchlorate in drinking water. Moreover, a recent study led by the Authority (Snyder, Stanford et al. 2009) has demonstrated that the use of hypochlorite for the disinfection of water may contribute perchlorate at levels within the range of HRLs shown in the FR. Therefore, we urge the EPA to consider the consequences of suggesting HRLs that do not consider epidemiological data that include in utero perchlorate exposure.

Response: EPA has carefully considered epidemiological data for perchlorate and determined that perchlorate meets SDWA's criteria for regulating a contaminant.

EPA agrees that perchlorate is naturally occurring. A 2006 study by a Texas Tech researcher (Dasgupta et al., 2006) identifies three principal sources of the perchlorate in the environment: its use as an oxidizer (rocket propellants, fireworks, flares and explosives), its presence in Chilean nitrate fertilizer, and formation via atmospheric processes.

Perchlorate is soluble and is taken up by plants along with water and nutrients. Its presence in food specifically is related to: (1) past propellant leakage into irrigation source water (e.g., Colorado River) which is applied to fields of crops that are distributed nationally; (2) smaller application of Chilean fertilizer to certain crops, i.e., principally in organic farming; and finally (3) rainfall and localized irrigation with ground water containing natural perchlorates.

Regarding the comment that the use of hypochlorite for the disinfection of water may contribute perchlorate at levels within the range of HRLs shown in the FR, EPA agrees that perchlorate has been found as an impurity in sodium hypochlorite which is commonly used by public water systems as a disinfectant to inactivate pathogenic micro-organisms. Reported concentrations of perchlorate introduced as a result of disinfection using sodium hypochlorite range from 1 ppb to 8 ppb (Greiner et al., 2008).

The extent to which perchlorate could be introduced into water from sodium hypochlorite depends on the operational practices of water utilities. In particular, the longer sodium hypochlorite is stored, the greater the concentration of perchlorate. These risk/risk tradeoffs can be addressed by implementing best management practices including storage in the dark at cool temperatures and use within 45 days of its manufacturing date. Perchlorate contamination resulting from sodium hypochlorite usage is more likely to occur in small drinking water systems than large.

Commenter Name: Kate Sande
Commenter Organization: Minnesota Department of Health, Health Risk Assessment Section
EPA Document ID: EPA-HQ-OW-2009-0297-0663
EPA Comment ID: 28701
EPA Comment Code: 5225

Comment: The Health Risk Assessment Unit with the Minnesota Department of Health appreciates the opportunity to submit comments in regards to EPA's Drinking Water: Perchlorate Supplemental Request for Comments (Docket ID No: EPA-HQ- OW-2009-0297). Please see our detailed comments found in the attached document.

October 8, 2009

Response to U.S. EPA, Drinking Water: Perchlorate Supplemental Request for Comments Docket ID No: EPA-HQ-OW-2009-0297

The approach taken by the Minnesota Department of Health (MDH) to develop health-protective guidelines for groundwater is consistent with alternative approaches considered by the U.S. EPA in the development of a drinking water guideline for perchlorate. The approach used by MDH to develop health risk limits (HRLs) for drinking water are much more aligned with the process outlined by the EPA in the August 19, 2009 Federal Register announcement than the process described in the December 2008 Perchlorate Interim Drinking Water Health Advisory report.

MDH supports EPA's August 2009 re-evaluation of the process used to develop drinking water guidelines for perchlorate. The previous approach used by the EPA in Interim Health Advisory Report was inconsistent with EPA risk assessment guidance. The use of the PBPK model appeared to be used to justify perchlorate exposure in infants and young children at levels above the RfD, an approach we would not endorse as health protective. Additionally, MDH was concerned by the lack of consideration of life stage sensitivities in the interim report, especially the absence of appropriate intake rates that were protective of sensitive subpopulations.

Response: See response to comment code 5220 for a discussion of the HRLs. See response to comment ID 20432 under comment code 5220 for a discussion of the PBPK model.

Commenter Name: Kate Sande
Commenter Organization: Minnesota Department of Health, Health Risk Assessment Section
EPA Document ID: EPA-HQ-OW-2009-0297-0663
EPA Comment ID: 28702
EPA Comment Code: 5225

Comment: Our comments include a discussion about how MDH accounts for life-stages sensitivities when developing HRLs and how our approach compares with the alternative approaches EPA is considering for developing a perchlorate drinking water guideline. We have also included an example of how MDH would calculate a HRL for perchlorate using EPA's RfD of 0.0007 mg/kg-day and comments comparing the MDH drinking water guidelines and the alternative HRLs that EPA is considering (listed in Table 2, section III.B-3 of the Federal Register announcement).

Note: If this were a chemical review conducted by MDH, we would independently review the toxicological literature to derive our own RfD, which may not result in the same RfD adopted by EPA for perchlorate.

Section III, B-4.a - Request for comments about appropriate exposure values that consider sensitive life stages

Intake Rates MDH strongly supports EPA's reconsideration to use life-stage specific, high end (95th percentile) drinking water intake rates in the development of alternative HRLs. This is consistent with the approach used by MDH and EPA's recommendation to evaluate exposures that are shorter than chronic durations to account for higher intake rates than can occur during shorter periods (EPA, 2002). Additionally, MDH agrees with EPA's approach to use appropriate and relevant body weights for sensitive individuals when calculating intake rates.

To account for lower body weights and higher water intake rates by infants and young children during acute and short-term exposure durations, MDH uses an intake rate of 0.289 L/kg-day, based on the 95th percentile intake for an infant up to 3-months (EPA 2004 & EPA 2008a). The subchronic intake rate we use is 0.077 L/kg-day based on the time-weighted average of the 95th percentile intake from birth up to 8 years of age. The chronic intake rate used by MDH is 0.043 L/kg-day and is based on the time-weighted-average of the 95th percentile intake over approximately 70 years.

Response: See response to comment code 5220.

Commenter Name: Kate Sande
Commenter Organization: Minnesota Department of Health, Health Risk Assessment Section
EPA Document ID: EPA-HQ-OW-2009-0297-0663
EPA Comment ID: 28704
EPA Comment Code: 5225

Comment: Section III, B-4.b - Request for comments on the alternative HRLs in Table 2 and which would be an appropriate guideline

The formula used by MDH to calculate a non-cancer health protective drinking water guideline is:

Non-cancer Guidelineduration = (RfDduration x RSC x 1000) / Intake Rateduration

In the table below (Table 1) you will find the range of perchlorate concentrations in drinking water that MDH would derive based on our standard intake rates and relative source contributions described above for multiple exposure durations (acute, short-term, subchronic, and chronic). The drinking water concentrations derived below are for comparison purposes only and do no reflect current MDH guidance.

Table 1. MDH drinking water guidelines compared to EPA HRLs for perchlorate. [see PDF docket ID EPA-HQ-OW-2009-0297-0663]

*We adjusted the life stages used by MDH to conform to EPA's life stages listed in Table 2, section III.B-3 of the Federal Register announcement, however normally, MDH categorizes health guidelines by exposure durations as outlined in EPA's Reference Dose Process guidance (EPA, 2002).

**MDH does not calculate guidlines for each life stage listed in Table 2, section III.B-3 so we only included EPA HRLs that correspond to the life stages we consider at MDH. The EPA HRLs that were most appropriate for comparison were the ones calculated using the 95th percentile intake rates.

*** We felt a chronic MDH guideline provided the most appropriate comparison to EPA's HRL for pregnant women. The EPA HRL is higher than the MDH guideline because MDH used our default RSC of 0.2 and EPA used an RSC of 0.62.

Using the MDH HRL approach to calculate theoretical perchlorate drinking water guidelines resulted in a range of perchlorate concentrations of 1-3 ug/L which account for all life stages and sensitive subpopulations. Based on these concentrations, it is likely we would select 1 ug/L as the guideline to ensure the most sensitive individuals are protected. The EPA HRL of 2 ug/L for infants less than 3-months old is much more comparable to the MDH guideline than the interim HRL of 15 ug/L.

Section III, B-4.d Request for comments on the merits of the approach to derive HRLs for sensitive life stages based on the RfD combined the life stage specific exposure data

MDH agrees with the approach of developing HRLs based on the RfD combined with life stage specific exposure data. When developing an HRL, MDH conducts an independent review of the toxicological literature to develop an RfD and calculates a drinking water guideline using intake rates and relative source contributions that are protective of life-stage sensitivities.

MDH commends the alternative approaches described in the EPA Drinking Water: Perchlorate Supplemental Request for Comments announcement. They show that EPA is seriously weighing all life stages and highly exposed sensitive subpopulations in the development of a perchlorate HRL.

Thank you for the opportunity to comment. Please contact Kate Sande (651-201-4902) kate.sande@state.mn.us) with the Health Risk Assessment Section in the Environmental Health Division if you have any questions concerning these comments.

Attachment: References

References

Greer MA; Goodman G; Pleus RC, Greer SE. 2002. Health Effects Assessment for Environmental Perchlorate Contamination: The Dose Response for Inhibition of Thyroidal Radioiodine Uptake in Humans, Environmental Health Perspectives110(9): 927 - 937. URL: http://www.ehponline.org/members/2002/110p927-937greer/greer-full.html

Minnesota Department of Health (MDH). 2008. State of Need and Reasonableness, Technical Support Document for the Health Risk Limit Rules for Groundwater. State of Minnesota, Minnesota Department of Health. URL: http://www.health.state.mn.us/divs/eh/risk/rules/hrlsonar08.pdf

National Research Council (NRC). 2005. Health implications of perchlorate ingestion. The National Academy Press. URL: http://www.nap.edu/catalog.php?record_id=11202#toc

U.S. EPA. 2002. A Review of the Reference Dose and Reference Concentration Process. Risk Assessment Forum, December 2002. URL: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=55365

U.S. EPA. 2004. Estimated Per Capita Water Ingestion and Body Weight in the United States - An Update Based on Data Collected by the United States Department of Agriculture's 1994-1996 and 1998 Continuing Survey of Food Intakes by Individuals. Office of Water, and Office of Science and Technology, October 2004. URL: http://www.epa.gov/waterscience/criteria/drinking/percapita/2004.pdf

U.S. EPA. 2005. Reference Dose for Chronic Oral Exposure (RfD) for Perchlorate and Perchlorate Salts. Integrated Risk Information System, February 2005. URL: http://www.epa.gov/iris/subst/1007.htm

U.S. EPA. 2008a. Child-Specific Exposure Factors Handbook. National Center for Environmental Assessment, September 2008. URL: http://cfpub.epa.gov/ncea/CFM/recordisplay.cfm?deid=199243

U.S. EPA. 2008b. Interim Drinking Water Health Advisory for Perchlorate. Health and Ecological Criteria Division, Office of Science and Technology, and Office of Water, December 2008. URL: http://www.epa.gov/ogwdw000/contaminants/unregulated/pdfs/healthadvisory_perchlorate_interim.pdf

Response: See response to comment code 5220.

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)

EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 28752
EPA Comment Code: 5225

Comment: B. Alternative HRLs Based Upon Body Weight and Water Consumption of Other Life Stages 4. Request for Comments a. EPA requests comment on whether the alternative HRLs described in this notice appropriately take into account specific and appropriate exposure values for all potential sensitive life stages, including infants, children and the fetuses of pregnant women (rather than the 70 kg body weight and 2 liter per day consumption used for past regulatory determinations).

Comment B.4.a.1: The available data do not indicate a differential effect on potentially sensitive subpopulations (fetuses and neonates). Consequently, alternative HRLs should not be developed for a postulated sensitive sub- population (fetuses and neonates). Development of alternative HRLs for a postulated sensitive sub-population should be predicated on reasonably rigorous scientific evidence demonstrating the need for such specificity. The current reference dose approach is generally believed to be sufficiently conservative to prevent health impacts with a margin of safety. We understand that the EPA does not find a need to reevaluate the current EPA-adopted RfD of 0.7 ug/kg-day, which is a conservative and health-protective reference dose that has a 10-fold uncertainty factor applied to the point of departure to account for differences between healthy adults and the most sensitive population: fetuses of pregnant women who might have hypothyroidism or iodine deficiency. Therefore, the development of alternate HRLs appears unnecessary because the health of the most sensitive sub-population (fetuses and neonates) has already been considered in setting and adopting the RfD. The need for application of a second tier uncertainty factor has not been demonstrated by the available studies. Application of an appropriately calculated relative source contribution (RSC) term, as was conducted during development of the January 2009 Health Advisory (HA), appears adequate and appropriate.

It is recommended that EPA support the design and collection of additional clinical data to determine if additional refinement of the RfD is needed to further address health protection of these sub-populations.

b. EPA requests comment on the alternative HRLs in Table 2 and which of these values would be appropriate levels of health concern against which to compare the levels of perchlorate found in public water systems.

Comment B.4.b.1: The available evidence in human populations indicates that all of the values identified in Table 2 are likely to be protective against adverse health effects. The NDEP notes that the reference dose calculation includes a 10-fold uncertainty, which was applied to the point of departure during development of the RfD to account for differences between healthy adults and the most sensitive population. NDEP believes that, based upon the currently available data, there is not adequate scientific basis at this time to depart from the health-protective Health Advisory level of 15 ug/L. This health- protective value already incorporates a 10-fold uncertainty factor to account for differences between healthy adults and the most sensitive population: fetuses of pregnant women who might have hypothyroidism or iodide deficiency.

c. EPA requests comment on whether EPA used the best available and most appropriate data to estimate alternative HRLs in Table 2. EPA specifically requests comment on the drinking water

ingestion rates in Table 2 (denoted by footnote c) where the sample size does not meet the minimum data requirements as described in the "Third Report on Nutrition Monitoring in the United States" (LSRO, 1995). Does aggregate life stages (birth to 6 months, and women ages 15 - 44) address sample size limitation and still provide an accurate representation of the exposure to the most vulnerable life stages?

Comment B.4.c.1: The fact that some of the data sets relied upon do not meet the minimum data requirements is one of the inherent problems in trying to regulate to a specific subpopulation rather than for the general population. If there was reasonably rigorous scientific evidence supporting the need for such special treatment to be protective against perchlorate health effects, an exception to minimum data requirements might be reasonable. However, the absence of such evidence, including considerable human data not supporting specialized sensitive receptor concerns, makes it inappropriate to incorporate these data for perchlorate regulation. The EPA-adopted reference dose of 0.7 ug/kg-day is a conservative and health-protective reference dose that has a 10-fold uncertainty factor applied to the point of departure to account for differences between healthy adults and the most sensitive population: fetuses of pregnant women who might have hypothyroidism or iodide deficiency. Consequently, additional adjustments to the RSC assumptions represent a second source of multiplicative conservatism that appear unnecessary to protect the sensitive sub-population.

Comment B.4.c.2: Separating the data into aggregate life stages (birth to 6 months, and women ages 15 - 44) is not necessary as it provides no discernable value in the calculation of an HRL, HA, or MCL. Steps such as these (separating life stages and grouping some life stages as aggregate life stages) might be justified if there were data demonstrating a valid concern for adverse health effects of perchlorate at or near the adopted Health Advisory.

d. EPA requests comment on the merits of the approach described here of deriving HRLs for sensitive life stages based on the RfD combined with the life stage specific exposure data and whether there are other approaches that may be useful for deriving HRLs.

Comment B.4.d.1: The merits of deriving HRLs as described in the August 19, 2009 Federal Register Notice include greater specificity of the risk-based calculations to the receptor population presumed to be of greatest concern, and perhaps reduced uncertainty in the degree of public health protection. However; the need for such an approach for deriving alternate HRLs for perchlorate that is more refined and conservative is not clearly supported by the available scientific evidence.

Response: EPA does not believe that an HRL of 15 ug/L adequately accounts for the greater exposure to perchlorate on a per body weight basis that infants and developing children have in comparison to adults. This greater exposure is not accounted for within the RfD as the 10-fold uncertainty factor accounts for greater sensitivity to the same exposure, not the fact that a child is likely to be exposed to a greater dose on a per body weight basis. See response to comment code 5220. Regarding the use of exposure data that meet minimum data requirements, EPA has relied on aggregated infant life stage data (i.e., birth to six months) that meet minimum data requirements for calculating the 90th percentile. EPA believes that the 90th percentile values within sensitive life stages appropriately account for variation in consumption on a per body weight basis and are protective of highly exposed individuals in these life stages.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)

EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28803
EPA Comment Code: 5225

Comment: a. Whether alternative HRLs take into account specific and appropriate exposure values for all potentially sensitive life stages

NRDC response: It is appropriate for the HRL to account for an infant's body weight, an infant's dietary intake and relative source contribution from water, and other contaminants that share a common mode of toxicity to perchlorate.

A bodyweight assumption appropriate for an adult female does not protect fetuses, infants or children. For example, infants consume almost six times more water (and therefore contaminants) than adults, on average, in proportion to their body weight. Therefore, it would not be appropriate to use an adult body weight when converting a reference dose into a drinking water standard that is protective of infants and children.

Many infants are breastfed for at least part of their first year of life, and perchlorate from both water and food does enter breast milk. Therefore, the appropriate choice for the breastfeeding scenario is to use an RSC value that reflects perchlorate the mother is taking in through food and drinking water since she is the source for the infant's breast milk.

Response: See responses to comment codes 5210 and 5220.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28805
EPA Comment Code: 5225

Comment: b. On which of the alternative HRLs in Table 2 would be appropriate against which to compare levels of perchlorate in public water systems

NRDC response: A level of perchlorate below 1 ppb is required to adequately protect vulnerable newborn babies and their recommended sole source of nutrition, breast milk.

In June 2006, the State of Massachusetts Department of Environmental Protection (MA DEP) and its scientific advisors (MA DEP/DPH Advisory Committee) "unanimously concluded that [the RfD] did not fully account for the uncertainties surrounding science's understanding of perchlorate toxicity and exposures."[FN46: MA DEP, "Update To 'Perchlorate Toxicological Profile And Health Assessment'" March 2006, page xii.] Following recommendations from their scientific experts, MA DEP finalized an enforceable perchlorate Maximum Contaminant Level for drinking water and a perchlorate Cleanup Standard of 2 ppb based on a review and assessment of all data available at the time. Likely because the Blount (2006) data were not yet available, the MA DEP drinking water and cleanup standards failed to consider the special exposure patterns of infants born to low-iodide women, whom we now know are among the most at-risk population based on both high exposure and vulnerability to permanent and severe neurological impacts. Therefore, an MCL must be below 1 ppb to be truly health protective.

Response: See response to comment code 5220.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28827
EPA Comment Code: 5225

Comment: PART I

EPA's Alternative HRL analysis. It is not clear whether EPA's new analysis resulting in new health reference levels (HRLs) is a one-time approach unique to perchlorate, due to a particular concern about certain subpopulations as noted in the 2005 National Academies of Science, National Research Council (NAS) report, or a new approach for determining contaminant levels that are of a concern for public health at various life stages based on EPA's 2005 Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants (2005 Guidance) that will be applied to future regulations.

If it is EPA's intent to apply the 2005 Guidance in this way for future regulations then EPA should clearly state this. AMWA also believes that the analysis should be sent to NAS for review since this is the first time that the 2005 Guidance has been applied in an analysis with implications for rule development, which would have major implications for future rulemakings.

The analysis could be specific to perchlorate as the contaminant is unique with respect to its health endpoints. As suggested in the peer review document of the drinking water health advisory for perchlorate, "...the biological impacts of perchlorate are very different from those for chemical compounds which have direct target organ toxicity and/or do not directly affect the availability of an essential element for which homeostasis occurs."

AMWA requests that EPA clearly explain the applicability of the alternative HRL analysis when issuing a final regulatory determination on perchlorate.

In addition, if the most sensitive subpopulation is the fetus of iodide deficient pregnant women, is the analysis showing new HRLs for children focused on those children who are iodine deficient? AMWA requests that EPA make this clear in its final determination. AMWA also recommends that EPA should make clear in its final regulatory determination whether it still considers the fetuses of pregnant women who are iodine deficient to be the most sensitive subpopulation.

Finally, AMWA asks that EPA discuss the significance of the lack of bioaccumulation of perchlorate in the body as noted in Greer et al., 2002 and NAS, 2005 after exposure and how this is accounted for in its exposure estimates in the HRL analysis.

Response: EPA believes that alternative HRLs described in the August 2009 notice appropriately take into account specific and appropriate exposure values for infants, children and the fetuses of pregnant women (rather than the 70 kg body weight and 2 liter per day consumption used for past regulatory determinations). This analysis is applicable to perchlorate because individuals at these life stages are particularly sensitive to the effects of perchlorate.

EPA will consider using life stage specific exposure factors where the best available science indicates life stages are particulary sensitive.

EPA's analysis of HRLs does not assume bioaccumulation of perchlorate.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28830
EPA Comment Code: 5225

Comment: NOEL vs. NOAEL

The 2005 National Research Council report recommended an RfD of 0.0007 mg/kg by employing two margins of safety. The first was to use the point of departure as a conservative NOEL vs. a NOAEL. In addition, the report recommended applying an additional factor of 10 to protect all sensitive groups, including the fetuses of pregnant women with iodine deficiency and children and infants.

AMWA asks that EPA clearly explain the significance of the NOEL vs. NOAEL in the alternative analysis of HRLs, as it appears that the agency is compounding safety factors that already account for the sensitivity and variability between population groups.

Response: EPA has clearly and consistently explained the basis of departure for the perchlorate RfD using the NRC report language.

EPA does not believe that accounting for specific and appropriate exposure values for all potentially sensitive life stages, including infants, children and the fetuses of pregnant women "compounds," or "double-counts," the uncertainty factor that has already been applied.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28836
EPA Comment Code: 5225

Comment: 74 FR 41889: "EPA specifically requests comment on the drinking water ingestion rates in Table 2 where the sample size does not meet the minimum data requirements as described in the "Third Report on Nutrition Monitoring in the United States (LRSO, 1995)."

Response: AMWA believes that if the sample sizes for estimates of ingestion rates in Table 2 do not meet minimum data requirements set forth in CDC's LRSO, then they should not be used for HRL development that could be used as a basis for national policy.

Response: As EPA states in the August 2009 notice, for six life stages in Table 2 (birth to < 1 month, 1 to < 3 months, 3 to < 6 months, 16 to 18 years and 18 to 21 years and for pregnant women), the sample size used to estimate some of the drinking water ingestion rates (denoted in

Table 2 by foot note "c") do not meet the minimum data requirements as described in the "Third Report on Nutrition Monitoring in the United States." However, these are the best available data to characterize drinking water ingestion for these specific life stages. EPA also notes that these data clearly show the trend that drinking water mean ingestion rate on a per body weight basis increases as the life stage age decreases. Although the approach may have shortcomings, EPA interpolations/extrapolations are reasonable and in accordance sound and objective scientific practices.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28840
EPA Comment Code: 5225

Comment: In closing, AMWA again urges EPA to have the alternative HRL and PBPK analysis reviewed as it is a new analysis that was developed by applying for the first time the 2005 Guidance. The potential precedent that will be set if these analyses are used in rulemaking will have significant ramifications for how future drinking water policy is developed. In addition, AMWA recommends that EPA consider all available science as well as the most recent occurrence data as it prepares its final regulatory decision.

If you have any questions about these comments, please contact me or Erica Brown, Director of Regulatory Affairs and Scientific Program Development at 202-331-2820 or via email: brown@amwa.net.

Sincerely,

Diane VanDe Hei Executive Director Cc: Peter Silva, OW Cynthia Doughtery, OGWDW Eric Burneson, OGWDW Attachment [see PDF docket ID EPA-HQ-OW-2009-0297-0494]
Response: EPA has evaluated the available science to inform the regulatory determination.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0415
EPA Comment ID: 28843
EPA Comment Code: 5225

Comment: Interpretation of the Physiologically-Based Pharmacokinetic (PBPK) Modeling

AWWA recognizes the value of using models for risk assessment purposes. The Agency, in response to concerns raised in October 2008, elected to reassess exposure to life stages and broaden the scope of "the most sensitive population" which previously had been defined by the National Research Council (2005) as "the fetuses of pregnant women who might have hypothyroidism or iodine deficiency." The assessment appropriately follows EPA's Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants (USEPA, 2005) which recommends the following 10 age groups be considered in exposure assessments for children.

- Less than 12 Months old: birth to < 1 month, 1 to < 3 months, 3 to < 6 months and 6 to < 12 months. - Greater than 12 months old: 1 to < 2 years, 2 to < 3 years, 3 to < 6 years, 6 to < 11 years, 11 to < 16 years, and 16 to < 21 years.

AWWA recognizes these important subpopulations, yet is troubled by the lack of recognition in the modeling efforts to incorporate the findings from the most recent and well designed epidemiological studies. These studies provide direct dose-response assessments that should be included into the Agency's modeling effort rather than making presumptive calculations for purposes of estimating a Health Reference Level (HRL) for each life stage examined. The majority of these studies have shown no adverse health effects to women of child bearing age, newborns, and school age children who were exposed to significant amounts of perchlorate via drinking water at levels below and above the EPA accepted Reference Dose (RfD) of 0.0007 mg/Kg-day), as well as to other goitrogens. These studies also address the request for comment regarding the use of the PBPK model to "explore the relative sensitivity of various life stages".

Response: See response to comment ID 28338 under comment code 5225.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0415
EPA Comment ID: 28845
EPA Comment Code: 5225

Comment: Alternative HRLs Based Upon Body Weight and Water Consumption of Other Life Stages

AWWA believes that it is unnecessary for the Agency to adjust for Relative Source Contribution (RSC) when calculating a HRL, since the RfD is based on a No Observed Effects Level (NOEL) and the Greer [FN7: Greer, M., Goodman, G., Pleus, R., and Greer, S. 2002. Health effects assessment for environmental perchlorate contamination: the dose-response for inhibition of thyroidal radioiodine uptake in humans. Environmental Health Perspectives, 110:927.] study only measured the incremental exposure to drinking water. The body of data on which the National Research Council (NRC) based their conclusions produced a No Observed Effects Level (NOEL) (not considered a No Observed Adverse Effects Level [NOAEL]because the biochemical changes measured were not considered adverse in and of themselves) of 0.007 mg/Kg-day. The NRC further recommended a total uncertainty factor of 10 for intraspecies extrapolation (the data were from humans), resulting in a recommended RfD of:

RfD = 0.007 / 10 = 0.0007 mg/Kg-day

The Agency [FN8: USEPA. 2005. EPA Sets Reference Dose for Perchlorate. New release dated 02/18/2005.
http://yosemite.epa.gov/opa/admpress.nsf/b1ab9f485b098972852562e7004dc686/c1a57d 2077c4bfda85256fac0 05b8b32!OpenDocument] accepted the NRC's RfD. Typically the RfD would be multiplied by the RSC for ingestion of drinking water to obtain a limit on exposure. However, this practice arose from the common use of clinical, epidemiological, or experimental animal studies in which individuals were exposed solely through the route of interest (e.g. ingestion of water). Given a sole route of exposure it is necessary to correct for the fact that individuals in the general

population would likely be exposed to a compound through multiple routes. As a result, the application of an RSC in the regulatory process is based on the (often unstated, but nonetheless implicit) assumption that the study population was NOT exposed through routes other than the one of interest, while the general population was exposed through ALL routes.

This assumption is not fully warranted in the case of perchlorate because the individuals in the Greer study maintained a normal diet during the period of the study.[FN9: Crawford-Brown, D., Raucher, B., and M. Herrod 2006. Inter-Subject variability of risk from perchlorate in community water supplies. Environmental Health Perspectives, 114:7:975.] Therefore, they should have been exposed to perchlorate from non-drinking-water routes at an Average Daily Rate of Intake (ADRI) value roughly equivalent to that of the general population that is the target of regulatory determinations. This is supported by the FDA's Total Diet Study [FN10: Murray, C.W III, S.K. Egan, H. Kim, N. Beru, P.M. Bolger. 2008. US Food and Drug Administration's Total Diet Study: Dietary Intake of Perchlorate and Iodine. Journal of Exposure Science and Environmental Epidemiology 18:571.] and the NHANES assessments [FN11: Blount, B.C., J.L. Pirkle, J.D. Osterloh, L. Valentín-Blasini, and K.L. Caldwell. 2006. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environmental Health Perspectives. 114:12:1865.],[FN12: Blount, B.C., L. Valentin-Blasini, J.D. Osterloh, J.P. Mauldin, and J.L. Pirkle. 2007. Perchlorate Exposure of the US Population, 2001-2002. Journal of Exposure Science and Environmental Epidemiology 17:400.], which suggests a ubiquitous exposure to perchlorate from various food sources. If this is the case, application of an RSC would in effect "double count" the influence of the non- drinking-water exposures, because the NOEL from the Greer study already reflected these background exposures (absent these background exposures, the NOEL of 0.007 mg/Kg-day would be expected to be higher).

Since the RfD is based on a NOEL versus the traditional NOAEL, EPA is already building in extra levels of protection. The current request for comments recognizes that this is a departure from the traditional approach and that the NOEL which is based on "using a nonadverse effect that is upstream of the adverse effect is a more conservative and health protective approach". The NRC's use of a precursor to an adverse effect is represented in Figure 1. The RfD represents a point of departure (POD) that precedes the inhibition of iodine uptake by the thyroid.

Figure 2 provides a generic representation of the difference between the NOEL and NOAEL. Given the very conservative and precautionary nature of the RfD, further adjustment of the RfD as suggested by the Agency for purposes of recommending HRLs is unwarranted. This is further supported by the epidemiological studies that cover multiple life stages at perchlorate levels above and below the suggested HRLs and observed no adverse effects.

Figure 1. Depiction of Point of Departure (POD) used to derive NOEL [see PDF docket ID EPA-HQ-OW-2009-0297-0415]

Figure 2. Perchlorate RfD represents a conservative point of departure (POD) for hazard assessment [see PDF docket ID EPA-HQ-OW-2009-0297-0415]

Response: See response to comment code 5210.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection (MassDEP)

EPA Document ID: EPA-HQ-OW-2009-0297-0495
EPA Comment ID: 28862
EPA Comment Code: 5225

Comment: 4) MassDEP supports setting the HRL on the basis of the life stage(s) with highest exposure and risk with a 90% percentile ingestion rate, which is standard practice. Based on Table 2, this would support an HRL of 2 ppb (or perhaps somewhat lower depending on the exposure estimate for the 7-day old). It is worthwhile to note that the alternative HRLs calculated using the 95th percentile exposure values for early life stages are not very different than the HRL values estimated using the 90th percentile ingestion rates, especially considering the rounding involved in the final calculation of the HRLs. Although EPA's concern about sample size and aggregation of life stages is legitimate, the aggregation of life stages in the current document (birth to < 6 months) yield closely similar HRL values derived for life stages birth to < 1 month, 1 to < 3 months, and 3 < 6 months and birth < 6 months and therefore appear to be reasonably stable estimates (Table 2).

Response: See response to comment code 5220.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection (MassDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0495
EPA Comment ID: 28864
EPA Comment Code: 5225

Comment: 6) We believe that EPA has used the best available exposure data for deriving the HRLs. Use of the 90% percentile ingestion rate addresses uncertainties regarding the issue of minimum data set deficiencies for ingestion rates.

Response: EPA has selected HRLs based on the 90th percentile ingestion rates as a basis for the final regulatory determination.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28869
EPA Comment Code: 5225

Comment: 2. Derivation of alternative Health Reference Levels (HRLs) based upon body weight and water consumption rates for sensitive life stages: The alternative HRL calculation which relies on life-stage specific body weight and water consumption rates is not scientifically justified. Authoritative bodies (e.g., NRC, EPA, the Agency for Toxic Substances and Disease Registry, the California Environmental Protection Agency Office of Environmental Health Hazard Assessment (OEHHA)) have conducted rigorous scientific assessments and have determined that the fetus of the hypothyroid pregnant woman is the most sensitive to perchlorate's potential health effects, not the infant as suggested by the alternative HRL calculation. The Notice provides no scientific evidence that shows otherwise and offers no justification for basing a HRL on an alternative population that is not the most sensitive. Further, the values given in the Notice for specific exposure assumptions do not meet the Agency's own guidelines for data quality.

Response: See response to comment ID 28752 under comment code 5225 for a discussion of considering life stage specific exposure data in calculating HRLs.

Regarding the comment that the values given in the notice for specific exposure assumptions do not meet the Agency's own guidelines for data quality, see response to comment ID 28836 under comment code 5225.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28879
EPA Comment Code: 5225

Comment: II. RESPONSES TO REQUEST FOR COMMENTS ON ALTERNATIVE APPROACHES TO ANALYZING SCIENTIFIC DATA RELATED TO PERCHLORATE IN DRINKING WATER

Compared to the EPA PBPK model, the alternative HRLs listed in the Notice are not scientifically rigorous.

The Agency's process is not transparent in how it might use any of the three alternative approaches described in the Notice to revise its regulatory determination for perchlorate. For example, the Notice does not remark if it intends to use both the PBPK model and the HRL "model." Further, the Notice is not clear about how the Agency intends to integrate the results of these alternative approaches with existing knowledge about the threshold for IUI in average adults.

The comments in this document assume EPA does not intend to apply both the PBPK model and alternative HRLs based on body weight and water consumption. Further, this document assumes that EPA seeks input on whether one approach is scientifically more accurate than the other for extrapolating from a no effect dose measured in adults to sensitive subpopulations. Overall, the scientific community supports the use of PBPK modeling when all parameters are based on scientific experiments (Mager et al., 2003). When scientifically validated, PBPK models can be useful to reduce uncertainty about sensitive life stages. In contrast and as will be discussed below, the HRLs based on body weights and water consumption rates do not reflect a similar scientific basis.

It is important to note the difference between the results in Table 1 of the Notice (which presents the PBPK model-predicted RAIU inhibition for each life stage) and Table 2 (which presents the alternative HRLs based on body weight and water consumption). The RAIU inhibition estimates in Table 1 were computed using a dose of 0.007 mg/kg-d, the Greer et al. (2002) POD. This dose is equivalent to 245 ppb of perchlorate in drinking water if one uses standard EPA default values for body weight and drinking water consumption.[FN7: 0.007 mg/kg-d x (70 kg adult / drinking 2 L of water per day = 0.245 mg/L or 0.245 ppm or 245 ppb.] The HRLs in Table 2 are based on the perchlorate RfD which is ten times lower, i.e., 0.0007 mg/kg-d or 24.5 ppb. Therefore, anyone comparing Tables 1 and 2 should recognize a 10-fold difference in the underlying dose assumptions. For example, the highest RAIU inhibition reported in Table 1 is 12.5% for the lactating woman and breast-fed infant exposed to a dose of 0.007 mg/kg-d. At the 10-fold lower RfD in Table 2, the RAIU inhibition for the lactating woman and breast-fed infant would be approximately 2%, a value

that would not be significantly different from normal fluctuations because of differences in diet and feeding styles. There is no credible scientific evidence that this effect has any biological significance.

Based on the EPA PBPK model, at the RfD, the RAIU inhibition for the exclusively breast-fed infant would be approximately 2%, a value that would not be significantly different from normal fluctuations due to diet.

Response: EPA was transparent in our August 2009 discussion of how we might consider the alternative HRLs in lieu of the single HRL of 15 ug/L used for the October 2008 notice. The agency was also clear that we were reconsidering our application of the PBPK model in light of how the comments we had received from both our peer reviewers and the commentors on the notice. See response to comment ID 28923 under comment code 2400 for a discussion of our decision not to use the PBPK modeling to inform the final regulatory determination.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28886
EPA Comment Code: 5225

Comment: B. Derivation of Alternative HRLs Based on Body Weight and Water Consumption Rates for Sensitive Life Stases

The NRC panel and subsequent studies consistently identify the fetus as the most sensitive population for perchlorate health effects evaluation.

In October 2008, EPA calculated an HRL for perchlorate in drinking water based on the RfD and a RSC of 62%, and EPA's default body weight and water consumption rates for an adult (U.S. EPA, 2008a). Based on a comment regarding the adequacy of EPA's proposed HRL to be protective of sensitive life stages, EPA presented an alternative calculation of an HRL in the Notice based on weight-normalized water intakes for specific life stages.[FN13: For example, EPA says, "One commenter cites a March 8, 2006, letter from the Children's Health Protection Advisory Committee to the EPA Administrator. The commenter states, "[T]he committee emphasized the higher exposure of infants to perchlorate and greater susceptibility to serious negative effects associated with perchlorate exposure. Neither of these issues, however, was given adequate consideration in the Preliminary Determination."] EPA has not presented any scientific evidence for why its proposed HRL in October 2008 was inadequate to protect other life stages or why it would be necessary to add additional safety factors to the RfD in the form of life stage-specific intake rates. In contrast to the PBPK model, the alternative HRL approach:

* is based primarily on one variable (the water intake rate);

* uses data that are not derived from scientific experiments but from a summary obtained in a survey that relies on subject recall rather than direct measurement;

* relies on methods that are incapable of measuring, estimating, or predicting the effects of a chemical on the body; and

* produces results that are qualitative at best.

In summary, determining the most sensitive life stages based on water consumption rates implicitly makes general assumptions about numerous body functions in lieu of actual scientific data about physiological differences between these population groups. This "model" does not account for absorption, distribution, or excretion, regardless of the individual's state of development. It implicitly assumes that the potential for exposure is directly proportional to body weight, without scientific supporting data.

PBPK modeling provides a more scientifically defensible approach to characterize the relative sensitivity of different life stages to perchlorate exposure. The Notice's alternative HRL calculations are insensitive, duplicative, and not scientifically warranted.

The Notice should be transparent that the alternative HRL calculation it presents is an arithmetic calculation based on only three variables: the RfD, an RSC, and life stage specific water intake rates. Of these, the only scientifically defensible value is that upon which the RfD is based- the POD derived from Greer et al. (2002). The RSC is based on the mean intake of perchlorate from the Food and Drug Administration (FDA) Total Diet Study for the nearest age range, and the 90th percentile intake from a NHANES-UCMR analysis for pregnant women and women ages 15-44 that was conducted for preliminary regulatory determination. Using the 90th percentile is a not a science-driven decision. The water intake by body weight is arbitrarily categorized by age (i.e., what is physiologically unique about 6 months of age versus 5 months of age?). Further, the consumption values for the infant are based on a study in which the study participant had to recall their own (or their infant's) consumption over two non-consecutive days; no direct measurements were taken. Recall studies are subject to error (called recall bias) from lapses in memory on estimations of amounts consumed (i.e., what, when, and how much did I eat or drink?). In addition, the population size in this study does not meet EPA's data quality standards.

The EPA has asked for comment on four general questions regarding the Notice's alternative HRL calculations. Responses to these questions, based on the best available scientific information, follow.

1. EPA requests comment on whether the alternative HRLs described in this notice appropriately take into account specific and appropriate exposure values for all potentially sensitive life stages, including infants, children and the fetuses of pregnant women (rather than the 70 kg body weight and 2 liter per day consumption used for past regulatory determinations).

The HRL methodology that the Notice describes does not appropriately account for sensitive life stages for several reasons: (1) the most sensitive population has already been considered in the perchlorate RfD; (2) EPA provides no scientific justification for why this alternative HRL is necessary; and (3) there are no scientific data that meet EPA data quality requirements to substantiate the calculations used to develop these HRLs.

Response: The NRC (2005) identified "the fetuses of pregnant women who might have hypothyroidism or iodide deficiency" as "the most sensitive population," but also identified infants and developing children as additional "sensitive populations." Infants and young children have greater exposure to contaminants in food and water because of greater consumption of food and water on a per unit body weight basis. Therefore, these life stages may be the most vulnerable populations when their relative exposure is considered. Therefore, EPA used this approach to derive

HRLs by evaluating exposures at different life stages. See response to comment ID 28752 under comment code 5225 for more discussion.

EPA believes that data to evaluate drinking water consumption on a per body weight basis are critical for comparison to the RfD for perchlorate. EPA further believes that the exposure data used by the Agency are the best available peer reviewed data.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28888
EPA Comment Code: 5225

Comment: The historic standard procedure for converting the RfD into drinking water equivalent levels (DWELs) assumes 2 liters (67.6 oz) per day of water consumption and a body weight of 70 kg (154 lbs). One important purpose of converting the RfD (in units of mg/kg-day) to a DWEL (in units of ug/L or ppb) is to make it easy to compare water concentrations of contaminants to government guidelines. In doing so, EPA conservatively opts for higher than average intake and lower than average body weight. Thus, these default values are not symmetrically representative of the population. The water consumption (2 liters) default is approximately equal to the 88th percentile water intake for adults aged 20 through 64 (U.S. EPA, 1997). The default body weight of 70 kg is approximately equal to the 27th percentile of the distribution for adult males aged 18-74 and the 70th percentile of the distribution for adult females (U.S. EPA, 1997). Because the conversion uses the ratio of body weight to water intake, the use of lower percentiles in the numerator than are used in the denominator leads to a biased overestimate of the dose.

The DWEL is based on the RfD. The RfD is defined as (NRC, 2005):

...an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or BMD, with UFs generally applied to reflect limitations of the data used.

Therefore, by definition, the RfD already accounts for the most sensitive population and lifetime exposures. In the most recent review of the RfD process, the EPA technical committee recommended (U.S. EPA, 2002):

The intraspecies UF is applied to account for variations in susceptibility within the human population (interhuman variability) and the possibility (given a lack of relevant data) that the database available is not representative of the dose/exposure-response relationship in the subgroups of the human population that are most sensitive to the health hazards of the chemical being assessed. As the reference concentration/dose is defined to be applicable to "susceptible subgroups," this UF was established to account for uncertainty in that regard.

EPA remarks that additional factors should not be applied to determine a MCLG. For example, in the Disinfectant and Disinfection Byproduct rule (enacted during the Clinton Administration), EPA rejected additional safety factors for children or adjusting the default adult body-weight/consumption parameters:

EPA disagrees that an additional safety factor should be applied to provide additional protection for children or that drinking water consumption relative to body weight of children should be used in developing the MCLG (maximum contaminant limit goal). The MCLG presented for chlorite and chlorine dioxide are considered to be protective of susceptible groups, including children, given that the RfD is based on a NOAEL derived from developmental testing. Additionally, current methods for developing RfDs are designed to be protective for sensitive populations. The 2 liter per day water consumption and the 70 kg body weight assumptions are viewed as adequately protective of all groups (U.S. EPA, 1998b).

Lifetime exposure includes exposure during infancy. An RfD that failed to account for exposure during infancy would fail to satisfy the standard definition. Applying life stage specific drinking water values would, in effect, "double count" the UF that has already been applied.

EPA requests comment on the alternative HRLs in Table 2 and which of these values would be appropriate levels of health concern against which to compare the levels of perchlorate found in public water systems.

The calculated values presented in Table 2 are not scientifically justified. Although this table presents levels that have been found in public water systems, there is no health effect associated with the values presented. In fact, every life stage calculation in Table 2 corresponds to a no effect level, based on IUI which is a fully reversible, nonadverse effect that occurs on a routine and daily basis.

The NRC noted that the dose at which perchlorate might cause hypothyroidism is greater than 0.4 mg/kg-d (14,000 ppb using default drinking water and body weight conversions). It states (NRC, 2005):

On the basis of the studies of long-term treatment of hyperthyroidism in which patients continued to be given perchlorate after their hyperthyroidism resolved and the clinical studies of healthy adults, the perchlorate dose required to cause hypothyroidism in adults would probably be more than 0.40 mg/kg per day, assuming a 70-kg body weight.

Importantly, the NRC (2005) also emphasizes:

The committee emphasizes that inhibition of iodide uptake by the thyroid has been the only consistently documented effect of perchlorate exposure in humans. The continuum of possible effects of iodide-uptake inhibition caused by perchlorate exposure is only proposed and has not been demonstrated in humans exposed to perchlorate (with the exception that in patients with hyperthyroidism doses of 200 mg daily or higher may reduce thyroid secretion).

The PBPK results, as presented in Table 1 of the Notice, show the 1 week old breastfeeding infant to have the greatest RAIU inhibition when its mother is given a dose 10 times greater than the RfD (e.g., exposure at water concentration of 245 ppb). This assumes that the infant would be exclusively breastfed. In calculating the HRL, the age groups that had the greatest intake per body weight, however, were the youngest infants who are exclusively formula fed. Based on the PBPK model, the bottle fed infant had a 1.5% change in RAIU inhibition, which is well within the normal variation of RAIU inhibition.

2. EPA requests comment on whether EPA used the best available and most appropriate data to estimate alternative HRLs in Table 2 (denoted by footnote c) where the sample size does not meet the minimum data requirements as described in the "Third Report on Nutrition Monitoring in the United States" (LSRO, 1995). Does aggregating life stages (birth to 6 months, and women ages 15-44) address sample size limitation and still provide an accurate representation of the exposure to the most vulnerable life stages?

The drinking water intake rates in the age groups are based on USDA Continuing Study of Food Intakes by Individuals from 1994-1996 and 1998. This was a large study of dietary recall and was reported by Kahn and Stralka (2008). Although this may be the best study that the Agency could find, it is neither sufficient nor does it meet the scientific standards the EPA's own guidelines demand for a regulatory process.

First, compared to the science-based data used in a PBPK model, water intake is an insensitive variable. It cannot be used for measuring, estimating, or predicting the effects of a chemical on the body. In fact, it does not and cannot estimate or predict any effects in the body. This study is not based on a specific experiment, but a summary of data obtained in a survey based on recall rather than direct measurements. The best and most scientific process would be to measure and record the exact amount of fluid or food intake at the time of ingestion.

Second, as noted by EPA in the Notice, for some life stages, the data do not meet EPA guidelines on data quality.[FN14: The Notice states "The sample sizes for the estimates of ingestion rates for these life stages do not meet the minimum data requirements as described in the "Third Report on Nutrition Monitoring in the United States" (LSRO, 1995)."] Water intake as the sole variable makes general assumptions about numerous body functions in lieu of actual data. For example, in effect, this calculation does not account for absorption, distribution, or excretion, regardless of developmental state. This calculation implicitly assumes that the body's disposition of perchlorate is directly proportional to body weight. There are no scientific data to support these assumptions.

Third, the study population in Kahn and Stralka (2008) may not be representative of the U.S. population. The body weights presented by Kahn and Stralka (2008) are lower than that found in 1996-2000 NHANES data, as presented by EPA in the Child Specific Exposure Factors Handbook (U.S. EPA, 2008d) and may not be representative of the general population. For one month olds, the Kahn and Stralka (2008) mean, 90th and 95th percentile body weights are 20, 45, and 24% lower than the NHANES 1996-2000 data. A greater body weight will result in a lower total dose, if intake is the same. The comparison body weights for the three youngest age groups are presented in Table 1 in Appendix A.

Fourth, Kahn and Stralka (2008) is a recall study. As noted above, this is a study in which the study participant had to recall their own (or their infant's) consumption over two non-consecutive days. No direct measurements were taken. Recall studies are subject to bias from errors in memory when recalling the amounts consumed (i.e., what, when, and how much did I eat or drink?). For example, it is possible and not unusual that the person reporting the infant intake estimated a high value for intake. If this occurred for one or two individuals in the study, the data would be skewed (as observed by inspection), overestimating the statistical estimation of the 90th and 95th percentile water consumption values.

Applying life stage specific drinking water values is, in effect, "double counting" the uncertainty factor that has already been applied.

Furthermore, a dietary recall study should represent the entire population, not just tap water consumers. The water intake from Kahn and Stralka (2008) were calculated based on individual parameters. EPA chose to use the data for consumers of water only, yet individuals commonly use water from other sources (e.g., bottled, in juice or soda). Since the EPA is interested in developing a MCL, sources of water that would be regulated are municipal water systems. One effect of choosing not to use the analysis of all individuals is that the results are higher than what would be reflected if all data were used. That is to say, this would not be a science-based decision. The results of using ingestion rates from consumer versus all individuals on the alternative HRLs are presented in Table 2 in Appendix A. To illustrate the effect noted above of limiting the population, in infants less than one month of age, the proposed alternative HAL based on consumers only was 3 ug/L; if the value for all individuals is used, the water concentration would be 8 ug/L.

EPA reports intake rates and alternative HRLs based on the mean, 90th, and 95th percentiles. Kahn and Stralka (2008) lack sufficient study size and methodology to reliably inform the science related to the general population, as the Notice acknowledges.

One way to gauge whether the 90th and 95th percentile values suggested in the Notice are statistically unreliable is a simple comparison to blood volume. The average adult has a blood volume of approximately 5 L and drinks approximately 1.4 L/d, or 27% of their blood volume (U.S. EPA, 1997). It is well understood that infants and children consume more than adults when normalized for body weight, but using the intake rates suggested by EPA, the 95th percentile one month old infant would consume 2.6 L/d or 280% of their blood volume. This is the equivalent of the average adult consuming just under 4 gallons, every day. Comparisons of water intake to blood volume are presented in Appendix A, Table 3.

The RfD is based on the study by Greer et al. (2002) and the researchers in this study did not control dietary intake of perchlorate or other natural agents such as nitrate, thiocyanate, or iodine. Perchlorate has been detected in many foods, including but not limited to milk, lettuce, and cantaloupe (Murray et al., 2008). No perchlorate was reported detected in Portland's city water supply (the location of the study) according to UCMR1. Thus, assuming that Murray et al, (2008), is correct, subjects would have received perchlorate from food (See Figure 1). Therefore, the dose of perchlorate that resulted in a NOEL was in addition to the background level of perchlorate ingested through food. If the background dose of perchlorate from all sources was 0.02 to 0.234 ug/kg-d (the 5th and 95th percentile estimated doses from Blount et al. (2007)), then all doses in Greer et al. (2002) underestimate the true dose by this amount and the RSC has already been considered.

Figure 1. Visual representation of UF, the RfD, and unaccounted for contribution of perchlorate in food are components of the POD dose. [see PDF docket ID EPA- HQ-OW-2009-0297-0662]

3. EPA requests comment on the merits of the approach described here of deriving HRLs for sensitive life stages based on the RfD combined with the life stage specific exposure data and whether there are other approaches that may be useful for deriving HRLs.

Given the strength of the underlying science in the EPA PBPK model, the proposed HRLs in the Notice do not address sensitive life stages in a scientifically justified manner.

Some have suggested that perchlorate should be regulated differently because its acute effects may be detrimental during sensitive life stages. This assumes that the UF applied to the RfD is not large enough to account for the most sensitive life stage. Such a claim would be not supported by scientific evidence. First, toxicologically speaking, an acute effect is an effect seen after one high dose or an exposure of less than 24 hours. No published study has demonstrated an effect after one exposure to perchlorate at environmental levels. Even if acute is meant to refer to effects over several weeks to months (more commonly termed "subchronic") of exposure, no study demonstrates adverse effects at environmental levels, nor would an effect be expected based on the current scientific literature. As the Greer et al. (2002) study demonstrated, any IUI at the POD dose is within normal variation and there is no evidence that any effects, much less any adverse effects, would be expected at doses near the RfD, on a short-term or chronic (lifetime) basis.

Response: See response to comment ID 28752 under comment code 5225 for a discussion of the use of life stage specific exposure values for determining HRLs. See response to comment code 5210 for a discussion of the relative source contribution. See response to comment ID 28338 under comment code 5225 for a discussion of the health implications of exposure above the RfD.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28903
EPA Comment Code: 5225

Comment: 2. The proposed use of alternative HRLs based upon body weight and water consumption of other life stages is not a scientifically-based process. If there were a lack of data for a particular chemical, then perhaps this approach would be defensible. For perchlorate, however, where the effort of scientists to reduce uncertainty has been long standing and focused, the use of body weight and water consumption would increase uncertainty. The PBPK modeling provides greater and more biologically significant information.

Response: See response to comment ID 20432 under comment code 5220 for a discussion of EPA's decision regarding the use of the PBPK model in the regulatory determination.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Department of Environmental Protection (NJDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0527
EPA Comment ID: 28911
EPA Comment Code: 5225

Comment: Alternative HRLs Based Upon Body Weight and Water Consumption of Other Life Stages

In the October 10, 2008 notice, the proposed Health Reference Level (HRL) for perchlorate of 15 ug/L was derived using exposure assumptions for a pregnant woman/fetus exposed to the RfD of 0.7 ug/kg/day with a Relative Source Contribution (RSC) factor of 0.6. In developing this HRL, USEPA assumed that the fetus is the most sensitive subpopulation, more sensitive than the infant, so that the infant could be safely exposed to much higher doses than the fetus.

We strongly disagree with the assumption that exposure of infants to perchlorate above the Reference Dose is acceptable. We urge USEPA to use exposure assumptions for all potentially sensitive life stages, especially infants and children, to derive alternative HRLs that are protective of all sensitive subgroups. A similar approach that considers exposure assumptions for infants was used by the NJDWQI (2005) in developing its recommendation for a perchlorate MCL, and by NJDEP (2009) in developing its MCL proposal. We strongly support USEPA's approach based on combining the RfD, which is intended to protect sensitive subpopulations, with exposure data specific for sensitive life stages such as infants. We do not advocate other approaches for deriving HRLs.

Response: See response to comment code 5220.

Commenter Name: Danielle Blacet
Commenter Organization: Association of California Water Agencies
EPA Document ID: EPA-HQ-OW-2009-0297-0208
EPA Comment ID: 28924
EPA Comment Code: 5225

Comment: 2) Alternative Health Reference Levels (page 41889)

ACWA has reviewed the table referenced in the request for comments and we believe that an educated answer is not feasible as the various levels are not based on science connecting exposure to any actual observed adverse health effect. We encourage USEPA to seek out or initiate studies that may better inform such a significant dataset.

Response: See response to comment code 5220.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group (EWG)
EPA Document ID: EPA-HQ-OW-2009-0297-0499
EPA Comment ID: 28929
EPA Comment Code: 5225

Comment: On August 19, the agency published a notice in the Federal Register seeking comments on its additional approaches to analyzing data related to its perchlorate regulatory determination. These new approaches differ from EPA's prior assessment primarily because they focus on the risks of perchlorate exposure to infants and children, as opposed to the prior assessment that focused on risks to the fetus of the hypothyroid or iodide-deficient woman. EWG fully supports these approaches. Although fetal development is a highly vulnerable life stage for perchlorate exposure, research from the last several years has confirmed that infants and children are an equally high-risk population group due to their small size relative to adults and their high level of perchlorate exposure via water and food.

Response: See response to comment code 5220.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group (EWG)

EPA Document ID: EPA-HQ-OW-2009-0297-0499
EPA Comment ID: 28931
EPA Comment Code: 5225

Comment: Appropriateness of alternative HRLs: EWG supports the alternative HRLs if they are modified to reflect risks to infants from widespread perchlorate contamination of powdered infant formula and if infants under six months of age are not aggregated in the agency's exposure assessment.

Further in its assessment, the agency also lists a number of new Health Reference Levels (HRLs) as an alternative to its proposed HRL of 15 ppb from December, 2008. The agency derived these new HRLs by evaluating exposure to perchlorate at different life stages. In Table 2 of the notice, the Agency lists HRLs for 14 different life stages at three different drinking water ingestion rates (average, 90th, and 95th percentile).

Ten of the life stages are for children 16 years old or younger, indicating the Agency's recognition that perchlorate exposures vary during each stage of childhood.

For drinking water ingestion rates at the 90th and 95th percentile rates for infants in the three youngest life stages, the Agency notes that the sample sizes for the estimates of ingestion rates do not meet established minimum data requirements. The actual sample sizes for these three groups are 37 (birth to <1 month), 108 (1 to < 3 months), and 269 (3 to <6 months). While they may not meet minimum data requirements, EWG strongly supports their use because these are the best data available (EPA 2008), and because aggregating these age groups masks significant exposure disparities in these critical life stages.

Infants in the youngest two life stages (birth to <1month and 1 to <3 months) have especially high drinking water ingestion rates. HRLs derived from the aggregated life stage of birth to <6 months would place some of the very young infants at high risk of exceeding the current RfD. For example, the HRL for the aggregated life stage at the mean ingestion rate is 4 ug/L. This would leave infants under three months of age at high risk of exceeding the RfD because they require an HRL of 3 or less to limit cumulative exposure below the RfD.

The HRLs are lowest for children ages two and under, consistent with the published data showing that infants and children have high baseline perchlorate exposures from food and relatively high water ingestion rates; therefore, infants and young children can easily exceed the current RfD by drinking tap water contaminated with even very small concentrations of perchlorate (Murray et al 2008, EWG 2008). For infants six months of age and under, the agency estimates HRLs from 1 to 5 parts per billion, depending on the exact age and mean drinking water ingestion rate.

Response: See response to comment code 5220.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection (MassDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0495
EPA Comment ID: 29098
EPA Comment Code: 5225

Comment: 3) Other sensitive populations should not be forgotten when EPA is addressing levels of health concern and potential numbers of people exposed to perchlorate in drinking water. Other sensitive subgroups not explicitly addressed include individuals with low iodine intake, untreated thyroid conditions, those suffering from cardiovascular and renal diseases (Miller et al. 2009; Iglesias and Diez 2009), individuals exposed to mixtures of other thyroid stressors, the elderly who are often prone to thyroid problems, and people with thyroid cancer. The results of Blount et al 2006 also indicate that women should be considered a sensitive group, certainly at the current RfD.

Response: EPA has calculated HRLs for women ages 15-44 as part of the final regulatory determination.

EPA agrees that these are sensitive groups and will consider them during the rulemaking process.

EPA Comment Code: 5230 Calculation of frequency of exposure above the HRL among pregnant women

Individual Comments
Commenter Name: Gregg Grunenfelder
Commenter Organization: Washington State Department of Health; and Oregon Department of Human Services
EPA Document ID: EPA-HQ-OW-2008-0692-1529
EPA Comment ID: 20457
EPA Comment Code: 5230

Comment: Table 2 presents a subset of EPA developed estimates of the population served by water systems for which the highest reported perchlorate concentration was greater than various threshold concentrations ranging from 4 ug/L to 25 ug/L. If lower threshold values derived from California, New Jersey, or Massachusetts were applied, the estimated number of potential exposed population would greatly increase. No value was estimated for a threshold corresponding to Massachusetts MCL of 2 ug/L, but is likely to be doubled that projected for a threshold value of 4 ug/L with greater than 30 million people within the United States potentially served by Public Water Systems with at least one detection greater than the threshold. The population estimates for entry or sample points having at least one detection greater than the threshold would likely be over 10 million, half of whom are female and greater than 210,000 may be pregnant at anyone time.

[Table 2. Occurrence and Population Estimates for Perchlorate Above Various thresholds - see PDF Docket ID EPA-HQ-OW-2008-0692-1529]

Response: Please see response to comment code 5220.

Commenter Name: Robert Howd
Commenter Organization: California Environmental Protection Agency, Water Toxicology Section
EPA Document ID: EPA-HQ-OW-2008-0692-1671
EPA Comment ID: 20649
EPA Comment Code: 5230

Comment: IV (B)(4), p 60277. The calculation of frequency of exposure makes the argument that a small proportion of women is pregnant at any one time, and therefore the percentage of the population at risk is quite limited, and there is no meaningful opportunity for a health risk reduction. This calculation ignores the fact that every individual is born of a pregnant female, and therefore the entire population of exposed individuals can be at risk at a critical formative period. The logical flaw in the EPA argument was to count pregnant females as at risk, rather than their fetuses, which assumes the effect is transient (in the pregnant females) rather than potentially permanent (in their offspring).

Response: Please see response to comment code 5220.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group

EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20916
EPA Comment Code: 5230

Comment: However, even with the many errors, flaws, and omissions in EPA's assessment, EPA still estimates that up to 2 million people throughout the U.S. could potentially be consuming water with levels of perchlorate that exceed this HRL. Here is EPA's exact statement:

"EPA's best estimate is that 0.9 million people (with an upper bound estimate of 2 million people) may be consuming water containing perchlorate at levels that could exceed the HRL for perchlorate and the Agency estimates that fewer than 30,000 of them are pregnant women at any given time" (EPA 2008).

It is astounding that EPA does not think it is necessary to set a stringent drinking water standard for perchlorate in order to protect 30,000 pregnancies annually. In addition, the 2 million people at risk include infants and children, so the subpopulations within this number that would benefit from a stringent drinking water standard would far exceed 30,000.

Response: Please see response to comment code 5220.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21101
EPA Comment Code: 5230

Comment: VIII. EPA Should Publish a More Accurate Estimate of the Population Exposed above the HRL in the Final Determination

In the proposed determination, EPA estimates that 16,000 pregnant women may consume drinking water with concentrations above the HRL of 15 ppb. It was appropriate to estimate pregnant women, because although we all begin life as a fetus, the fetal exposure period is finite and an individual becomes less susceptible to the effects of possible reduced thyroid function as he ages. The actual number is likely to be much lower than the estimate in the proposed determination.

Response: Please see response to comment code 5220.

EPA Comment Code: 5240 Consideration of other sensitive subpopulations (e.g., infants, children, and persons with iodine deficiency or thyroid disorders) when establishing the HRL

Individual Comments
Commenter Name: Melanie A. Marty, Ph.D.
Commenter Organization: Children's Health Protection Advisory Committee
EPA Document ID: EPA-HQ-OW-2008-0692-0962
EPA Comment ID: 20419
EPA Comment Code: 5240

Comment: A number of states have recently established perchlorate drinking water standards or goals that are more appropriate than USEPA's HRL published in the Oct 10th FR notice. The New Jersey MCL is 5 ug/L, the California Public Health Goal is 6 ug/L and the Massachusetts MCL is 2 ug/L. These drinking water values were intended to keep perchlorate exposures below the RfD for all groups including young children. Approximately 4% of public water supplies serving 17 million Americans would be in exci.edance of an HRL between 2 and 6 ug/L. This is 15 million more at risk individuals than currently estimated by the Agency. Thus, the proposed HRL of 15 ug/L has the potential to leave large numbers of infants inadequately protected against perchlorate.

Response: EPA has determined that perchlorate meets the criteria for regulating a contaminant in Section 1412(b)(1)(A) of SDWA. When EPA proposes the NPDWR for perchlorate, the Agency will also propose a Maximum Contaminant Level Goal (MCLG) for perchlorate. See response to comment code 5220.

Commenter Name: Carol Bigelow
Commenter Organization: University of Massachusetts
EPA Document ID: EPA-HQ-OW-2008-0692-1427
EPA Comment ID: 20627
EPA Comment Code: 5240

Comment: Perchlorate interferes with thyroid function in both animals and humans. A consideration of known differences in thyroid physiology between adults and neonates/infants supports the conclusion that the neonate and infant are the most "at risk" population.

Three important differences in thyroid physiology between adults and neonates/infants supports the conclusion that this population is the most vulnerable to perchlorate exposure (reviewed by (Ginsberg et al., 2007)):

1) Serum half-life of the thyroid hormone T4 is substantially longer in the adult relative to the neonate (7-10 days (Chopra and Sabatino, 2000)) versus 3 days (Lewander et al., 1989; van den Hove et al., 1999). This means that for adults, serum thyroid hormone levels are stable in the face of the daily fluctuations in perchlorate exposure and iodine uptake that might arise from drinking water contaminated with perchlorate. In contrast, the shorter serum half-life of T4 in the neonate means that there will be a much more rapid response to the inhibition of iodine uptake by perchlorate.

2) The adult thyroid gland stores a considerable amount of hormone, possibly enough for several months of normal secretion (Greer et al., 2002). Consequently, adults can presumably function normally without new hormone synthesis for extended periods. In contrast, the neonatal thyroid gland contains essentially no extra hormone and the amount of thyroid hormone in the neonatal gland represents a single day's worth of hormone (van den Hove et al., 1999). Therefore, the neonate must generate new hormone on a daily basis and perturbations in iodine uptake can have significant consequences.

3) The adult thyroid system can compensate for low thyroid hormone levels and the consequences of low thyroid hormone are likely to be reversible. This is in contrast to the neonatal thyroid gland which does not readily compensate for low thyroid hormone (reviewed by (Ginsberg et al., 2007)), and the consequences of low thyroid hormone at this time are not reversible (reviewed by (Rovet, 2002; Zoeller and Rovet, 2004).

Thus, neonates and infants represent unique "at risk" populations in the matter of perchlorate exposure and its effects on public health.

Response: See response to comment code 5220.

Commenter Name: Carol Bigelow
Commenter Organization: University of Massachusetts
EPA Document ID: EPA-HQ-OW-2008-0692-1427
EPA Comment ID: 20632
EPA Comment Code: 5240

Comment: Considering that the Blount study (Blount et al., 2006a) is the only study available to the EPA that had the ability to identify a relationship between life-time, low-dose perchlorate exposure and thyroid function, this study should supercede the Greer 2002 study for the derivation of the RfD. This study demonstrates that, in women with low urinary iodide, perchlorate exposure at the 50th percentile is associated with a 1.06 ug/dL reduction in serum total T4. While this may be of uncertain clinical significance to adult women, it is clinically significant to an infant during highly sensitive periods of postnatal brain development. In addition, the EPA would then be in a stronger position because it would be regulating on hormone reduction, rather than iodide uptake inhibition. Moreover, it is now conclusively shown that perchlorate is transported by the sodium/iodide symporter (NIS) (Dohan et al., 2007) and is found at high levels in human milk (Kirk et al., 2007; Pearce et al., 2007). Thus, the US EPA should recalculate the RfD and HRL based on the CDC study as the point of departure.

Response: See response to comment ID 29096 under comment code 5220.

Commenter Name: Lenny Siegel
Commenter Organization: Center for Public Environmental Oversight
EPA Document ID: EPA-HQ-OW-2008-0692-2019
EPA Comment ID: 20853
EPA Comment Code: 5240

Comment: November 24, 2008

US Environmental Protection Agency Office of Water Docket (Mail Code: 2822T) 1200 Pennsylvania Avenue, NW Washington, DC 20460

Ref: Docket EPA-HQ-OW-2008-068

Dear Sirs/Mmes:

In the October 10, 2008 Federal Register EPA made a preliminary determination that not enough people in the United States are exposed to significant levels of perchlorate in public drinking water systems to merit the issuance a national primary drinking water regulation. This is one of the most disappointing and convoluted EPA documents that I have ever reviewed.

To reach that conclusion, it proposes to specify a health reference level of 15 parts per billion (ppb) based on its current reference dose of .7 micrograms per kilogram per day and a calculation of dietary sources of perchlorate other than drinking water. As other commenters have explained, EPA has failed to recognize that this health reference level exposes young children to levels of perchlorate above the reference dose.

Response: See response to comment code 5220.

Commenter Name: Apparent Mass Mailing #6 - Earth Justice
EPA Document ID: EPA-HQ-OW-2008-0692-0972
EPA Comment ID: 20885
EPA Comment Code: 5240

Comment: Many experts disagree with your assessment that drinking water with 15 parts per billion of perchlorate is safe and acceptable. Scientists from the California Environmental Protection Agency and the Massachusetts Department of Environmental Protection have set stricter standards to will ensure that the most vulnerable populations -- pregnant women, infants, and small children -- are protected from the adverse impacts of perchlorate.

Response: See response to comment code 5220.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20905
EPA Comment Code: 5240

Comment: * EPA continues to consider pregnant women to be the population most at risk and ignores recent evidence that breast-fed infants and young children are the most highly exposed populations;

Response: See response to comment code 5220.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432

EPA Comment ID: 20913
EPA Comment Code: 5240

Comment: EPA focuses on risks to pregnant women while ignoring evidence of risks to breastfed infants and young children: There have been at least four published studies that highlight widespread perchlorate contamination of human breast milk. The most recent of these also postulated that perchlorate is preferentially excreted into breast milk when compared with iodine. Just as troubling, the average levels of perchlorate in breast milk in these studies would expose a significant number of breast fed infants to perchlorate levels above EPA RfD of 0.7 ug/kg/day. Breast fed infants do not get thyroid hormones through breast milk and must produce these hormones themselves; they are completely dependent on maternal iodine for thyroid hormone production and perchlorate exposure through breast milk could significantly inhibit this process. Adequate levels of thyroid hormones during infancy are integral to normal growth and brain development.

Yet, despite growing evidence that breast fed infants are one of the most highly exposed populations and are uniquely vulnerable to perchlorate, EPA chooses to ignore this data. EPA does not even acknowledge this population as being at risk. In fact, EPA notes that "The subpopulation that is the most sensitive to perchlorate exposure is the fetus of the iodine-deficient pregnant women" while ignoring the evidence of risks to infants (EPA 2008).

Similarly, young children are also highly exposed to perchlorate; FDA found that perchlorate contaminates 74% of 300 commonly consumed foods and beverages (Murray et al. 2008). It is well established that children eat and drink more, pound for pound, than adults. For this reason, perchlorate contamination of food is especially concerning for young children. FDA finds that among 2 year olds, perchlorate exposures from contaminated food and beverages alone fall between 50 and 56% of EPA RfD of 0.7 ug/kg/day (Murray et al. 2008). EWG analysis of FDA data finds that additional exposures to perchlorate from contaminated drinking water could easily result in combined exposures that exceed the EPA RfD. The average two year old will exceed EPA's RfD for perchlorate by drinking water that is contaminated with as little as 4 ppb of perchlorate (EWG 2008).

EPA does not explore risks to young children in any detail in their assessment, despite clear evidence from FDA research that perchlorate exposures from food are higher for young children than any other demographic group. As mentioned earlier, EPA focuses on the developing fetus of iodine-deficient pregnant women as the subpopulation that is at highest risk from perchlorate exposure while explicitly ignoring evidence that breast-fed infants and young children are also at risk.

Response: EPA believes the NRC appropriately based the RfD on iodide uptake inhibition to the thyroid, for the reasons discussed in its report. See response to comment ID 28927 under comment code 2110.

Commenter Name: Lucy Allen
Commenter Organization: Pacific Institute
EPA Document ID: EPA-HQ-OW-2008-0692-1770
EPA Comment ID: 20926
EPA Comment Code: 5240

Comment: Concern raised by the Children's Health Advisory Committee regarding the unique levels of exposure and developmental impacts of perchlorate on breast-fed infants were not addressed, and the reference dose[FN1: 0.7 ug/kg/day, or 49 ug/day for an adult weighing 70kg] upon which the EPA based the preliminary decision may not adequately protect the health of breast-fed infants. While the health risk posed by perchlorate to fetuses of pregnant women with hypothyroidism was considered in the preliminary regulatory determination, we are concerned that the health risk to breast-fed infants was not adequately addressed. Recommendations provided by the Children's Health Protection Advisory Committee (CHPAC) in its March 8, 2006 letter have not been appropriately adopted,[FN2: Children's Health Protection Advisory Committee. (2006, March 8). Letter to Stephen L. Johnson, EPA Administrator. Accessed Oct. 28, 2008 from http://www.ewg.org/files/chpac-epa_ltr.pdf.] which is especially disconcerting in light of the U.S. Government Accountability Office's (GAO) recent finding that the EPA has routinely failed to respond to this committee's findings.[FN3: U.S. Government Accountability Office (GAO). (2008). Environmental Health: EPA Efforts to Address Children's Health Issues Need Greater Focus, Direction, and Top-level Commitment. Accessed November 4, 2008 from http://www.gao.gov/new.items/d081155t.pdf.] Despite the EPA's recognition that children may be more vulnerable to environmental hazards, the GAO found that the EPA has failed to proactively seek advice from the CHPAC and "largely disregarded key recommendations" from the committee.[FN4: GAO. (2008). Environmental Health: EPA Efforts to Address Children's Health Issues Need Greater Focus, Direction, and Top Level Commitment. Retrieved Oct 27, 2008 from http://www.gao.gov/new.items/d081155t.pdf.] In the case of perchlorate, the committee emphasized the higher exposure of infants to perchlorate and greater susceptibility to serious negative effects associated with perchlorate exposure. Neither of these issues, however, was given adequate consideration in the Preliminary Determination.

* Perchlorate is actively transported into human breast milk where it concentrates, resulting in exposure levels above the reference dose for infants feeding on this milk. In the Preliminary Determination for perchlorate, the EPA used a reference dose designed to "estimate the daily oral dose that is likely to have no appreciable risk of deleterious effects during a lifetime"[FN5: National Research Council (NRC). (2005). Health Implications of Perchlorate Ingestion. Washington, D.C.: The National Academies Press, 208.] of 0.7 ug/kg/day. However, the CHPAC calculated that infants would be exposed to perchlorate levels approximately 5-10 times higher than this reference dose with a maternal exposure of 24.5 ug/L of perchlorate in water, plus a dietary intake of 8.4 ug/day. Because maternal exposure in this calculation is above the EPA's reference dose, we recalculated infant exposure with a total maternal perchlorate exposure equal to the reference dose (0.7 ug/kg/day). The results showed that a breast-fed infant would be exposed to approximately 5-8 times the reference dose.[FN6: Calculation of infant exposure to perchlorate: Nursing Infant Dose (ug/kg/d) = (ug/L in human milk/ug perchlorate ingestion-day) *[(24.5 ug perchlorate/L water)* (L water ingested/day)+ (baseline US dietary ingestion rate, ug/d)]*(L human milk ingested/day/infant body weight) Modified formula used by us to estimate infant exposure, with total maternal exposure equal to EPA's reference dose of 0.7 ug/kg/day (assuming adult body weight of 70 kilograms, as was used by EPA in the Preliminary Regulatory Determination): Maternal exposure: (0.7 ug/kg/day)*(70kg)= 49 ug/day Nursing Infant Dose (ug/kg/d) = (ug/L in human milk/ug perchlorate ingestion-day)*(49 ug/day)*(L human milk ingested/day/infant body weight) Aside from the maternal daily perchlorate exposure, we used the same parameter values as were used by the CHPAC. Please see the letter from CHPAC of March 8, 2006 for an explanation of these parameter values. Our infant exposure calculations: (0.458 day/L)*(49 ug/day)* (0.634 L milk/day/3.69 L) = 3.85 ug/kg/day (0.737 day/L)*(49 ug/day)* (0.634 L milk/day/3.69 L) = 6.20

ug/kg/day Calculation comparing infant exposure (calculated above) to the reference dose: 3.85 ug/kg/day / (0.7 ug/kg/day)= 5.5 6.20 ug/kg/day / (0.7 ug/kg/day)= 8.86]

* Infants are more susceptible to the serious neurological development effects of perchlorate, which can result in irreversible impacts. Due to their life stage, infants can suffer serious neurodevelopmental impacts because their central nervous system is still developing and is susceptible to small deficits of thyroid hormone level; they lack hormone reserves that adults have accumulated to buffer hormone deficits; and they may experience a slower clearance of perchlorate from their bodies.

Response: Since the NRC also identified infants and developing children as additional life stages, EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 µg/L to 47 µg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These HRLs are calculated based on individuals who consume an average amount of perchlorate from food (except for pregnant women where EPA used a 90th percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts. EPA is evaluating these potential alternative HRLs and considers them to be levels of public health concern for purposes of this determination.

Commenter Name: Caroline Baier-Anderson, PhD
Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20947
EPA Comment Code: 5240

Comment: Perchlorate and Iodine in infants

The CDC study does not capture either perchlorate exposure or thyroid hormone response in infants, which is an important sensitive subpopulation. A recent study measuring iodine intake in breastfeeding infants found that only 1 in 13 infants was receiving adequate levels iodine, based on Institute of Medicine Guidelines (Dasgupta et al. 2008). In fact, six infants in the lower half of the group were receiving only between 12 and 29% of the suggested intake values for iodine (Dasgupta et al 2008). In this same study, the ingestion of perchlorate in human milk exceeded the reference dose for perchlorate in 9 out of 13 infants. The concentrations of perchlorate and iodine reported in this study were generally similar to earlier studies, including Kirk et al. 2005 and 2007 and Blount et al. 2007.

Response: No response necessary to the information provided by the commenter.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20980
EPA Comment Code: 5240

Comment: In addition to its preliminary determination not to regulate perchlorate in drinking water, EPA has proposed an HRL of 15 micrograms/L (ug/L, equal to parts per billion, ppb) of perchlorate in drinking water, assuming 62% of the daily perchlorate dose comes from water, and the rest comes from food.[FN4: 73 Fed. Reg. at 60275.][FN5: Calculation of the HRL: For all populations, including pregnant women, the RfD is 0.7 ug/kg/day. EPA reports that for pregnant women, exposure to perchlorate from food is 0.263 ug/kg/day at the 90th percentile, representing nearly 38% of the RfD, and thus leaving an RSC (relative source contribution) for water of 62% (FR at 60276). This is equavelent to 0.437 ug/kg/day from water, assuming an average body weight of 70 kg, and a daily water consumption of 2 L. That is, 0.437 ug x 70 kg body wt. = 30.6 ug perchlorate in 2 L (the daily consumption amount). This is 15 ug/L, or 15 ppb, the HRL.] The HRL "will be the basis for the health advisory value in the health advisory document the Agency expects to issue at that time. Thereafter, it may be appropriate to use the health advisory value as a "to be considered" (TBC) value in developing potential cleanup levels for perchlorate at Superfund sites."[FN6: Id. at 60265.] The HRL is not protective of sensitive sub- populations and EPA's own scientists have produced strong evidence using PBPK modeling that this level of water contamination would mean bottle-fed infants would exceed the EPA reference dose or 'safe' level of 0.7 ug/kg/day by five- fold, and young children would exceed the reference dose by 2.8-fold (based on average food contamination rates, average body weights, and 90th percentile water consumption rates for each age group). Furthermore, EPA's HRL determination did not include consideration of a subpopulation that is likely to be highly exposed to perchlorate and uniquely sensitive: the breast-feeding neonate.

Response: See response to comment code 5210 for a discussion of the RSC and response to comment code 5220 for a discussion of HRLs.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20991
EPA Comment Code: 5240

Comment: B. EPA's analysis fails to consider the health risks perchlorate poses to key sensitive sub-populations.

EPA has stated in its preliminary determination that the most sensitive subpopulations are women of reproductive age and the fetus. This determination improperly excludes consideration of other sensitive subpopulations including pre-term infants, neonates and breast-feeding infants. Recent studies demonstrate that infants born to low-iodide women are the most at-risk population, because of both high dietary exposures and because infancy is a highly sensitive developmental stage. Disruptions to normal hormone activity during this time is likely to result in permanent abnormalities. EPA has not adequately accounted for this sub-population in its analysis or its PBPK modelling.

Infants are routinely being exposed to unsafe levels of perchlorate and a major route of exposure is through contaminated breast milk. A collaborative study from the CDC and Boston University examined breast milk samples from 49 Boston area women and found the median breast milk perchlorate level was 9.1 ppb (range 1.3 to 411 ppb).[FN25: EN Pearce, AM. Leung, BC Blount, HR

Bazrafshan, X He, S Pino, L Valentin-Blasini, and LE Braverman, 2007. Breast milk iodine and perchlorate concentrations in lactating Boston-area women. J Clin Endocrinol Metab. 92(5):1673-7.]

To make matters worse, the Boston study found that 47 percent of the babies tested were not getting adequate levels of iodine from breast milk. Since the effects of perchlorate are compounded by insufficient iodide consumption, these babies are at even greater risk for thyroid hormone disruption. Notably, the Boston study also found that even moms who ingested extra iodine by using iodized salt or taking multivitamins containing iodine did not always have sufficient iodine in their breast milk. This finding underscores the need for the government to take effective actions to significantly reduce perchlorate contamination of food and drinking water.

The Boston study also measured perchlorate concentrations in the mother's urine, finding a median level of 3.0 ppb. More important than the actual values, however, is the fact that these concentrations are remarkably similar to levels of perchlorate found in the much larger Centers for Disease Control and Prevention (CDC) study of perchlorate exposure that tested the urine of more than 2,800 individuals.[FN26: Blount BC, L Valentin-Blasini, JD Osterloh, JP Mauldin, and JL Pirkle. 2007. Perchlorate exposure of the US population, 2001-2002. J Expo Sci Environ Epidemiol. 17(4):400-7.] In that study, the median urinary perchlorate concentration was 3.6 ppb. Since the perchlorate exposures in the two studies are so closely aligned, one can assume that the high levels found in the Boston women's breast milk are, unfortunately, likely to be typical of the general U.S. population.

Response: See response to comment code 5220.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20993
EPA Comment Code: 5240

Comment: C. EPA ignores data showing that pre-birth and newborn infants are a highly vulnerable sub-population based on health impacts.

EPA's preliminary regulatory determination focuses on the number of pregnant women who are affected by perchlorate contamination; but this analysis ignores the fact that prebirth and newborns are also a highly vulnerable subpopulation.

An earlier analysis by scientists with the CDC of a nationally representative sample of 2,299 U.S. residents greater than 12 years of age has documented that exposure to perchlorate poses potential health risks to women of child-bearing age and especially to their babies (hereinafter referred to as "Blount (2006)").[FN29: Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environ Health Perspect. 2006 Dec;114(12):1865-71.] These data were not available at the time of the NRC review, but have since been published. This study tested the association of chronic perchlorate exposure, as measured by urinary perchlorate excretion, with total serum thyroxine (T4) concentration, and thyroid stimulating hormone (TSH) concentration.

For women with low iodine intake (defined by the World Health Organization as urinary iodine < 100 ug/L),[FN30: World Health Organization (WHO). 1994. Indicators for assessing iodine deficiency disorders and their control through salt iodization. WHO/NUT/94.7. Geneva: WHO/International Council for the Control of Iodine Deficiency Disorders.] very low levels of perchlorate exposure were associated with decreased serum T4 and increased serum TSH; the CDC estimates that 36% of U.S. women have iodine intakes in this range. For iodine-sufficient women (defined as urinary iodine >= 100 ug/L), perchlorate exposure was associated with increased TSH. Increased TSH is an indicator that the body is attempting to compensate for a decrease in thyroid hormone production, and is clinically considered to be a more sensitive marker of subtle thyroid alteration than depressed levels of serum T4. When predicting changes in serum TSH with increasing perchlorate exposures, women with low iodine intake and TSH levels on the high end of the normal range (> 3.11 IU/L) appeared to be the most sensitive group. In this group, any increase in urinary perchlorate predicted an increase in TSH that was consistently more than twice the predicted increase in TSH for women with low iodine levels and median TSH levels. For unknown reasons, perchlorate was not associated with T4 or TSH levels in men. The observed changes in serum T4 and TSH in women are consistent with our understanding of how thyroid hormones are regulated in the body, and with the mechanism of toxicity of perchlorate.

Importantly, the extremely low levels of perchlorate were associated with thyroid hormone disruptions - and the magnitude of these disruptions. The CDC researchers found that if a low iodine woman started with perchlorate exposure corresponding to 0.19 ppb in urine (the minimum level found), and then ingested enough perchlorate through food and/or drinking water to raise her urinary perchlorate level to 2.9 ppb (the median level found), her T4 levels would drop by 13%.[FN31: The drop in T4 predicted to be 1.06 ug/dL; the percentage decrease is calculated as compared to the average T4 level found in the CDC study (8.27 ug/dL).] Similarly, if her urinary perchlorate level increased to 5.2 ppb (the 75th percentile exposure), her T4 levels would drop by 16%. The maximum level of perchlorate exposure found was 100 ppb, which translated into a 29% decline in T4.

The unique physiology of pregnancy and interactions between the mother and fetus makes both especially susceptible to the harmful effects of perchlorate. Maternal T4 is the only source of thyroid hormone for the fetus in the first trimester. Recent studies have shown that the cognitive development of the fetus is impaired in mothers with even mild disruptions in thyroid hormone levels, prompting the medical community to recommend thyroid hormone replacement therapy for pregnant women who are found to have sub-clinical hypothyroidism (mildly elevated TSH but normal T4).[FN32: Cooper, D. 2004. Sub-clinical thyroid disease: consensus or conundrum. Clinical Endocrinology 60 (410-412); Haddow JE, Palomake GE, Allan, WC, Williams JR, Knight GJ, and Gagnon J, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. New England Journal of Medicine 1999: 341: 549-555; Pop VJ, Kuijpens J., van Baar, AL, Verkert, G. et al. 1999. Low maternal free thyroxine concentrations during early pregnancy are associated with impaired psychomotor development in infancy. Clinical Endocrinology 50 (149); Surks M., Ortiz E., Daniels G., Sawin C., Col N., Cobin R., Franklyn J. Hershman J., Burman K., Denke M., Gorman C., Cooper R., Weissman N. 2004. Subclinical Thyroid Disease. Subclinical Thyroid Disease. Journal of the American Medical Association 2004: 228-238.]

An analysis by Environmental Working Group reported that if the CDC's results for low iodine women with high-normal TSH levels are extrapolated to the general population, one would expect

more than 2 million women in the U.S. to become subclincally hypothyroidic as a result of drinking water contaminated with just 5 ppb of perchlorate.[FN33: Environmental Working Group. 2006. Thyroid Threat: Under Proposed Rocket Fuel Standards, Many Women Would Need Treatment To Protect Baby. Available at: http://www.ewg.org/node/20968] If these women became pregnant, they would require medical treatment to restore their thyroid hormones to normal levels and protect their babies from IQ deficits and abnormal development.

Response: See response to comment code 5220.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20995
EPA Comment Code: 5240

Comment: An MCL below 1 ppb is required to adequately protect vulnerable newborn babies and their recommended sole source of nutrition, breast milk

In June 2006, the State of Massachusetts (MA DEP) and its scientific advisors (MA DEP/DPH Advisory Committee) "unanimously concluded that [the RfD] did not fully account for the uncertainties surrounding science's understanding of perchlorate toxicity and exposures."[FN45: MA DEP, "Update To 'Perchlorate Toxicological Profile And Health Assessment'" March 2006, page xii.] Following recommendations from their scientific experts, MA DEP finalized a Perchlorate Maximum Contaminant Level for drinking water and a Perchlorate Cleanup Standard of 2 ppb based on a review and assessment of all data available at the time. Likely because the Blount (2006) data were not yet available, the MA DEP drinking water and cleanup standards failed to consider the special exposure patterns of infants born to low-iodide women, whom we now know are the most at- risk population based on both high exposure and vulnerability to permanent and severe neurological impacts. Therefore, an MCL must be below 1 ppb to be truly health protective.

Response: See response to comment code 6120.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 21006
EPA Comment Code: 5240

Comment: Furthermore, a maximum contaminant level below 1 ppb would afford reasonable protections to the health of the susceptible populations of pregnant women and breast-fed infants.

Response: See response to comment code 6120.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-2082
EPA Comment ID: 21018
EPA Comment Code: 5240

Comment: Having reviewed your letter in detail, I'll now address the specific issues raised.

1. You express concern with in utero and postnatal development, particularly neonates with greater exposure than adults and who lack stores of thyroid hormone.

Specifically, your letter states that EPA's HRL of 15 μg/L is a flawed benchmark and would allow daily exposures to infants that are 2-5 times higher than the Reference Dose (RfD) and that this lifestage must be adequately protected.

Based upon the conservative and health-protective NAS-based RfD and even more conservative Health Reference Level (HRL) benchmark, this lifestage will receive significant protection. The HRL relies on the NAS-recommended RfD that has several levels of caution built into calculation of the dose. The NAS report recommended an RfD of 0.7 μg/kg-d based on a level that causes no inhibition of iodine update or a No Observed Effect Level (NOEL)--the dose at which no effects occur, adverse or otherwise (NAS, 2005). The NAS panel stated that using a NOEL as the point of departure is a more conservative and health-protective approach than EPA's customary approach of using the adverse effect (i.e., using a dose at which there is no observable adverse effect level or the Lowest Observable Adverse Effect Level; (NAS, 2005). The NAS panel also took care to distinguish between a No Observable Adverse Effect Level (NOAEL) and a NOEL. The experts observed that there was confusion between the two and clarified that the NOAEL is based upon an adverse effect, whereas the NOEL is based upon a dose at which no effect occurs, adverse or otherwise. (NAS, 2005). EPA adopted the RfD recommended by the NAS and confirmed that it was conservatively based on the NOEL, not the NOAEL.

In using a NOEL, the NAS committee adopted a notably cautious, health-protective approach. In addition, the NOEL has an additional safety factor of 10 added this factor to ensure protection for the most sensitive individuals in a population, in this case, hypothyroid or iodine-deficient pregnant women and their developing fetuses. Importantly, the NAS panel did consider other sensitive populations in addition to pregnant women and their fetuses. They also considered the potential effect on infants, developing children, people who have compromised thyroid function, and people who are iodidedeficient. While it has been argued that the infant or child is the more sensitive individual in the population; experts from the NAS perchlorate panel, US EPA, CA OEHHA, and others agree that pregnant women and their fetuses are the most sensitive, thus these other sensitive groups would be protected if the most sensitive group is protected.

Response: The comment is addressed to the Children's Health Protection Advisory Committee, not to EPA, therefore, a response is not appropriate.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-2082
EPA Comment ID: 21023
EPA Comment Code: 5240

Comment: 6. Your letter states EPA's HRL is too high for infants and would allow daily exposures to infants that are 2-5 times higher than the RfD.

Perchlorate is not known or likely to occur in public water systems with high enough frequency nor does it occur at levels or public health concern. The NHANES studies and breast milk biomonitoring studies, notwithstanding their limitations, reveal that the US population is not exposed to levels of perchlorate that could cause an adverse effect, even when all exposure sources - in food and water - are considered. EPA's UCMR monitoring found a mean concentration of less than 10 ppb in systems with perchlorate - more than 100 times lower than the NAS' estimated effect level. Only a few systems have found any samples with concentrations greater than 100 ppb. Even the maximum level detected in the US is approximately 50 times lower than the dose at which the NAS panel estimated adverse effects could begin.

Response: The comment is addressed to the Children's Health Protection Advisory Committee, not to EPA, therefore, a response is not appropriate.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21099
EPA Comment Code: 5240

Comment: VI. Sensitive Subpopulations Could Be Exposed to Drinking Water with Greater than 15 ppb Perchlorate without Adverse Health Effects

As stated in these comments, in the Intertox summary, and in our comments to EPA's May 1st, 2007 notice, EPA should use an HRL equal to the RfD to reflect the conservative approach of the RfD and the ample evidence that exposure at the RfD have no effect on individuals, including sensitive subpopulations.

However, even if EPA uses its methodology in the final determination, EPA should use a larger Bin III subgroup to mitigate the potential limitations discussed previously. Using the sample group of females of childbearing age increases the sample size significantly. Switching the subpopulation of concern to women of childbearing age increases the sample size by five-fold, lowering the reliance on just a few observations. More importantly, it captures the subpopulation the NAS panel identified as the most sensitive - fetuses of women with low iodine consumption. The most critical period for the fetus in a woman with sustained iodine deficiency may even occur before she knows she is pregnant. As EPA notes, assigning one value for consumption, body weight, and other parameters to represent all of pregnancy is difficult. For these reasons, if EPA continues its approach, we recommend EPA use the HRL derived from the Bin III estimate of food consumption for all women of childbearing age.

Response: EPA agrees that would increase the population of interest from 97 to 503 but took a conservative approach in looking at women who knew they were pregnant during the NHANES survey. We also performed a curve fitting and an analysis to eliminate outliers. The calculated water dose of 0.559 vs 0.502 for pregnant women would have resulted in an HRL of 19 to 20 vs 15 using the pregnant population.

Commenter Name: Andria Ventura
Commenter Organization: Clean Water Action et al.
EPA Document ID: EPA-HQ-OW-2009-0297-0528

EPA Comment ID: 28513
EPA Comment Code: 5240

Comment: In responding to this threat, EPA must set a drinking water standard for perchlorate that protects the most vulnerable subpopulations, particularly pregnant women, fetuses, infants, and small children. By interfering with the thyroid's ability to take up iodide, perchlorate can suppress the development of thyroid hormones critical to growth, development, and metabolism. This puts fetuses and children at particular risk for learning and behavioral disabilities; impaired gait, vision, and hearing; and even mental retardation. Exposure calculations must therefore consider the ingestion rates for these populations, and the reference dose should consider the particular vulnerabilities of these age groups. EPA should also include in its calculations low birth weight babies and underweight infants, as these populations may be extremely vulnerable.

Response: See response to comment code 5220.

Commenter Name: Kathy Curtis
Commenter Organization: Alliance of Nurses for Healthy Environments (ANHE)
EPA Document ID: EPA-HQ-OW-2009-0297-0651
EPA Comment ID: 28544
EPA Comment Code: 5240

Comment: In responding to this threat, EPA must set a drinking water standard for perchlorate that protects the most vulnerable subpopulations, particularly pregnant women, fetuses, infants, and small children. By interfering with the thyroid's ability to take up iodide, perchlorate can suppress the development of thyroid hormones critical to growth, development, and metabolism. This puts children at particular risk for learning and behavioral disabilities; impaired gait, vision, and hearing; and even mental retardation. Exposure calculations must therefore consider the ingestion rates for these populations, and the reference dose should consider the particular vulnerabilities of these age groups. EPA should also include in its calculations low birth weight babies, and underweight infants as these populations may be extremely vulnerable.

Response: See response to comment code 5220.

Commenter Name: Diane Henshel
Commenter Organization: The School of Public and Environmental Affairs, Indiana University
EPA Document ID: EPA-HQ-OW-2009-0297-0492
EPA Comment ID: 28600
EPA Comment Code: 5240

Comment: We disagree with the currently recommended HRL of 15 ug/L in drinking water. We have done a landscape scale analysis of newborn Low Birth weight in California counties in which perchlorate was detected in drinking water in at least 2 samples. Total number of counties included in the analysis was 13. Interestingly, at least one of the counties which we considered to have relatively high levels of perchlorate in the drinking water was included as a reference county in another study using the same health data, but using different methods to determine effect.

We used regression analysis correlating the incidence of very low birth weight (LBW), as determined by the California Department of health services, with the mean concentration of perchlorate in the

drinking water samples in which perchlorate was at or above the detection limit. We found a statistically significant positive correlation between the presence of perchlorate- contaminated drinking water and LBW percentage at the population level, even when taking a measure of poverty (%uninsured) into account. Notably, there seems to be no threshold for LBW effects (although the lowest mean concentration evaluated was 3 parts per billion [ppb] perchlorate) and the relationship saturated by 10 ppb perchlorate in drinking water. Note that the effect of perchlorate on low birth weight appears to saturate below the EPA recommended HRL, and had no detectable threshold for the data used. (The detection limit was between 2 - 4 ug/L) Not only is the recommended HRL above a level at which there appears to be a positive correlation with increased incidence of LBW in newborns, but it is well above the saturating dose. Thus using 15 ug/L as an inflection point to analyze the differences in effects for populations exposed to perchlorate in DW above and below 15 ug/L would be biasing the results of the study towards artificially finding no effect of perchlorate on LBW (a false negative).

Diane Henshel dhenshel@indiana.edu

Attachment [See PDF Docket ID EPA-HQ-OW-2009-0297-0492; note this is copyrighted material]

Response: See response to comment code 5220.

Commenter Name: Nsedu O. Witherspoon
Commenter Organization: Children's Environmental Health Network
EPA Document ID: EPA-HQ-OW-2009-0297-0674
EPA Comment ID: 28736
EPA Comment Code: 5240

Comment: September 18, 2009

Water Docket Environmental Protection Agency Mailcode 2822T 1200 Pennsylvania Avenue, NW Washington, D.C. 20460

Re: Docket ID No. EPA-HQ-OW-2009-0297

Submitted via www.regulations.gov

The Children's Environmental Health Network (the Network) appreciates the opportunity to comment on the importance of regulating perchlorate in drinking water. We wish to associate ourselves with the comments submitted by Clean Water Action, the Center for Public Environmental Oversight et al on this topic.

The Network is a national organization whose mission is to promote a healthy environment and to protect the fetus and the child from environmental health hazards. The Network's Board and committee members include internationally- recognized experts in children's environmental health science and policy who serve on key Federal advisory panels and scientific boards. We recognize that children, in our society, have unique moral standing. The Children's Environmental Health Network was created to promote the incorporation of basic pediatric facts such as these in policy and practice:

* Children;s bodies and behaviors differ from adults. In general, they are more vulnerable than adults to toxic chemicals. * Children are growing. Pound for pound, children eat more food, drink more water and breathe more air than adults. Thus, they are likely to be more exposed to substances in their environment than are adults. Children have higher metabolic rates than adults and are different from adults in how their bodies absorb, detoxify and excrete toxicants. * Children's systems, including their nervous, reproductive, digestive, respiratory and immune systems, are developing. This process of development creates periods of vulnerability when toxic exposures may result in irreversible damage when the same exposure to a mature system may result in little or no damage. * Children behave differently than adults, leading to a different pattern of exposures to the world around them. For example, they exhibit hand-to-mouth behavior, ingesting whatever substances may be on their hands, toys, household items, and floors. Children play and live in a different space than do adults. For example, very young children spend hours close to the ground where there may be more exposure to toxicants in dust, soil, and carpets as well as low-lying vapors such as radon, mercury vapor or pesticides. * Children have a longer life expectancy than adults; thus they have more time to develop diseases with long latency periods that may be triggered by early environmental exposures, such as cancer or Parkinson's disease.

Clear, sound science underlies these principles. A solid consensus in the scientific community supports these concepts.

The world in which today's children live has changed tremendously from that of previous generations. There has been a phenomenal increase in the substances to which children are exposed. According to the EPA, more than 83,000 industrial chemicals are currently produced or imported into the United States. Thousands of chemicals are ubiquitous in our environment worldwide. Traces of hundreds of chemicals are found in all humans and animals. Every day, children are exposed to a mix of chemicals, most of them untested for their effects on developing systems. Many of these chemicals are readily passed across the placenta to the fetus, to the infant via breast milk, or via toys and other children's products. Many of these chemicals are also ingested in food and water. Many also are absorbed by children through the lungs by respiration of contaminated air.

Response: No response necessary to the information provided by the commenter.

Commenter Name: Nsedu O. Witherspoon
Commenter Organization: Children's Environmental Health Network
EPA Document ID: EPA-HQ-OW-2009-0297-0674
EPA Comment ID: 28738
EPA Comment Code: 5240

Comment: In responding to this threat, EPA must set a drinking water standard for perchlorate that protects the most vulnerable subpopulations, particularly pregnant women, fetuses, infants, and small children. By interfering with the thyroid's ability to take up iodide, perchlorate can suppress the development of thyroid hormones critical to growth, development, and metabolism. This puts fetuses and children at particular risk for learning and behavioral disabilities; impaired gait, vision, and hearing; and even mental retardation. Exposure calculations must therefore consider the ingestion rates for these populations, and the reference dose should consider the particular vulnerabilities of these age groups. EPA should also include in its calculations low birth weight babies, and underweight infants as these populations may be extremely vulnerable.

Response: See response to comment code 5220.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28815
EPA Comment Code: 5240

Comment: However, even if EPA proceeds with its determination not to regulate perchlorate and instead finalizes an HRL, that level must be adjusted to account for the actual data from the PBPK model showing that hundreds of thousands of infants would exceed the safe daily perchlorate intake levels at the proposed HRL.

These comments are respectfully submitted for your consideration,

Jennifer Sass, Ph.D. Mae Wu, JD

Response: See response to comment code 5220.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection (MassDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0495
EPA Comment ID: 28861
EPA Comment Code: 5240

Comment: Section III(B): Comments on Alternative Approaches for Calculating Health Reference Levels (HRLs)

1) MassDEP recommends that EPA use the approach to setting HRLs as shown in Section III, Subsection B-3.

2) We support EPA's reassessment of exposure assumptions for life stages, including fetuses of gestation week 40, infants and developing children. Application of EPA's Guidance on Selecting Age Groups for Monitoring and Assessing Childhood Exposures to Environmental Contaminants is appropriate along with application of EPA's Guidance for Risk Characterization to convey the variability in risk levels experienced by different individuals in the population. In doing so, EPA has appropriately taken into account specific and appropriate exposure values for many but not all potentially sensitive life stages. Because of the potential sensitivity of the early neonatal period from birth to several days thereafter, we believe that exposures to the bottle-fed 7- day old should also be considered. In EPA's Interim Drinking Water Health Advisory for Perchlorate, the 7-day old bottle-fed infant was estimated to have the highest perchlorate exposure per body weight.

Response: See response to comment code 5220. Since the NRC also identified infants and developing children as additional life stages, EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 μg/L to 47 μg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These HRLs are calculated

based on individuals who consume an average amount of perchlorate from food (except for pregnant women where EPA used a 90th percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts. EPA is evaluating these potential alternative HRLs and considers them to be levels of public health concern for purposes of this determination.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28876
EPA Comment Code: 5240

Comment: Vulnerable populations have been considered since the first risk assessment in 1998. All of EPA's interim guidance and the current RfD (which is the basis for the 2008 HRL) are based on the most sensitive subpopulation, the developing fetus.

A small percent of those who commented on EPA's preliminary regulatory determination opined that the infant or child is the most sensitive population to perchlorate health effects; however, experts, including authoritative bodies such as the National Academy of Sciences (NAS) National Research Council (NRC) perchlorate committee as well as federal and state agencies such as the EPA, the Agency for Toxic Substances and Disease Registry (ATSDR), the California Environmental Protection Agency Office of Environmental Health Hazard Assessment (OEHHA), and others, conclude that the fetus is the most sensitive population to protect (all others being less sensitive than the fetus are therefore protected). Furthermore, questions about alternative life stages being more sensitive to perchlorate exposure have been addressed in the past; EPA began focusing on the most sensitive life stage as the foundation of health protection as early as 1998 in its first risk assessment (U.S. EPA, 1998a).

Response: Since the NRC also identified infants and developing children as additional life stages, EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 µg/L to 47 µg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These HRLs are calculated based on individuals who consume an average amount of perchlorate from food (except for pregnant women where EPA used a 90th percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts. EPA is evaluating these potential alternative HRLs and considers them to be levels of public health concern for purposes of this determination.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28887
EPA Comment Code: 5240

Comment: Some have opined that the infant is the most sensitive individual in the population, but no scientific basis for this has been presented. The weight of evidence shows that the fetal brain is more sensitive to hypothyroidism than the neonate or infant brain (Boelaert and Franklyn, 2005).

There is no scientific evidence presented in the Notice that demonstrates that other life stages are more sensitive with regard to the development of health protective toxicity guidelines values than the fetus.

The NRC considered all possible sensitive populations in addition to pregnant women and their fetuses; this included infants, developing children, people who have compromised thyroid function, and people who are iodide-deficient, as sensitive to perchlorate exposure. Based on its assessment, the NRC committee states that "...fetuses and preterm newborns constitute the most sensitive populations although infants and developing children are also considered sensitive populations" (NRC, 2005). The purpose of defining an RfD based on "the most sensitive population" is that all other populations, including those that are more sensitive than average (but less sensitive than the most sensitive), would not be expected to have adverse effects, including at doses that exceed the RfD. To date-and with substantial scientific justification-the EPA, ATSDR, the states of California, Massachusetts, and New Jersey all regard fetuses to be the most sensitive population for health effects evaluations.

The RfD is an estimate or a representation of the acceptable level of risk for a lifetime of exposure. It is not a threshold above which adverse effects occur.

Reliable scientific studies published since NRC (2005) continue to demonstrate that no observable effect occurs at doses below the RfD. On a weight-of-evidence basis, the scientific literature demonstrates no significant health risk to the most sensitive individuals who consume water on a daily basis over a lifetime at environmentally relevant doses. Overall, these studies demonstrate that perchlorate is a ubiquitous chemical. It is naturally formed and is ubiquitous in the environment (Dasgupta et al., 2005), food (Murray et al., 2008), and the human body (Blount et al., 2006; Pearce et al., 2007b).

The RfD is an estimate of the acceptable level of risk for a lifetime of exposure. It is not a threshold above which adverse effects occur. This is particularly true for the perchlorate risk assessment which is based on a NOEL, a more conservative POD than a NOAEL or LOAEL. EPA is correct in setting acceptable exposure levels with margins of safety. This allows, for example, an individual to consume a dose above the RfD on one day and ingest a lower dose on a subsequent day. When considering perchlorate, the issue relative to other chemicals is less of a concern: perchlorate is not metabolized, does not bioaccumualate, and the half-life is approximately 8 hours. Thus, in the rare instance of an exceedence of the RfD over the short term, perchlorate leaves the body quickly. Currently, EPA's use of a ten-fold intraspecies factor in the RfD effectively covers the potential for differences in sensitivity and exposure.

The RfD is based on a NOEL for IUI. IUI is not adverse. It is not scientifically justified to use drinking water rates for specific life stages to lower the HRL when the current RfD already has an OF applied to account for the most sensitive individuals. EPA offers no justification for why other life stages might be currently at risk or why additional protection is needed. EPA remarks "The NRC (2005) identified 'the fetuses of pregnant women who might have hypothyroidism or iodide deficiency' as 'the most sensitive population,' but also identified infants and developing children as additional 'sensitive populations.'" The purpose of defining an RfD based on "the most sensitive population" is that all other populations, including those that are more sensitive than average, would not be expected to have adverse effects, including at doses that exceed the RfD. In addition,

reporting that the HRL could be lower in a group that is not the most sensitive without scientific support is not in compliance with the scientific method.

Bereft of scientific evidence, the Notice fails to present justification to alter the HRL based on specific life stages, particularly when the current RfD already has an uncertainty factor applied to account for the most sensitive individuals.

The purpose of defining an RfD based on "the most sensitive population" is that all other populations, even if they are more sensitive than average, would still be unlikely to suffer adverse effects, even at doses that exceed the RfD.

Response: EPA disagrees, the life stages at which individuals are most sensitive and therefore at greatest risk of adverse effect (the fetus, infant, and developing child) are inherently less than a lifetime. See response to comment ID 28338 under comment code 5225. Since the NRC also identified infants and developing children as additional life stages, EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 µg/L to 47 µg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These HRLs are calculated based on individuals who consume an average amount of perchlorate from food (except for pregnant women where EPA used a 90^{th} percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts. EPA is evaluating these potential alternative HRLs and considers them to be levels of public health concern for purposes of this determination. See response to comment 5220.

EPA Comment Code: 5300 SDWA Criterion #3 – EPA's determination that regulating perchlorate with a NPDWR would not represent a meaningful opportunity to reduce health risks for persons served by public water systems

Response to Code 5300: Using the criteria mandated by the 1996 SDWA Amendments EPA has determined that regulation of perchlorate in drinking water systems presents a meaningful opportunity to reduce health risk for persons served by public water systems and has decided to begin development of a national primary drinking water regulation for perchlorate. See response to comment code 6120.

Individual Comments
Commenter Name: Apparent Mass Mailing #1 - Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-0081
EPA Comment ID: 19688
EPA Comment Code: 5300

Comment: Setting a standard for perchlorate will absolutely present 'a meaningful opportunity for health risk reduction.' I urge you to do so in accordance with the Safe Drinking Water Act and protect Americans' health.

Response: See response to comment code 5300.

Commenter Name: Apparent Mass Mailing #1 - Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-0081
EPA Comment ID: 19688
EPA Comment Code: 5300

Comment: Setting a standard for perchlorate will absolutely present 'a meaningful opportunity for health risk reduction.' I urge you to do so in accordance with the Safe Drinking Water Act and protect Americans' health.

Response: See response to comment code 5300.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0117
EPA Comment ID: 19698
EPA Comment Code: 5300

Comment: Setting a standard for perchlorate will absolutely present 'a meaningful opportunity for health risk reduction.' I urge you to do so in accordance with the Safe Drinking Water Act and protect Americans' health.

Response: See response to comment code 5300.

Commenter Name: J Mason
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-0145
EPA Comment ID: 19727
EPA Comment Code: 5300

Comment: Setting a standard for perchlorate will absolutely present 'a meaningful opportunity for health risk reduction.' I urge you to do so in accordance with the Safe Drinking Water Act and protect Americans' health.

Response: See response to comment code 5300.

Commenter Name: A. Lane
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0276
EPA Comment ID: 19782
EPA Comment Code: 5300

Comment: Setting a standard for perchlorate will absolutely present 'a meaningful opportunity for health risk reduction.' I urge you to do so in accordance with the Safe Drinking Water Act and protect Americans' health.

Response: See response to comment code 5300.

Commenter Name: S. G. Gompf
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0490
EPA Comment ID: 19912
EPA Comment Code: 5300

Comment: By EPA's own data collection, perchlorate is present in drinking water in 35 states; by independent studies, the EPA has permitted up to 40 million Americans to be exposed to this harmful chemical.

Setting a standard for perchlorate is absolutely â€˜a meaningful opportunity for health risk reduction.â€™ I urge the EPA to do so in accordance with the Safe Drinking Water Act and protect the health of America's mothers and children.

Response: See response to comment code 5300.

Commenter Name: Rebecca Fletcher
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0530
EPA Comment ID: 19943
EPA Comment Code: 5300

Comment: We need to create standards for regulating the presence of this chemical in our water. Setting a standard for perchlorate will absolutely present â€˜a meaningful opportunity for health risk reduction.â€™ I urge you to do so in accordance with the Safe Drinking Water Act and protect Americansâ€™ health.

Thank you!

Wishing you good health, Rebecca Fletcher

Florence, MA 413-863-9038

Response: See response to comment code 5300.

Commenter Name: Margaret Baco
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0624
EPA Comment ID: 19997
EPA Comment Code: 5300

Comment: Setting a standard for perchlorate will absolutely present â€˜a meaningful opportunity for health risk reduction.â€™ I urge you to do so in accordance with the Safe Drinking Water Act and protect Americansâ€™ health. The absolute lowest level should be established immediately, with the commitment to essentially eliminate further contamination. Clean water is our greatest national resource.

Response: See response to comment code 5300.

Commenter Name: Apparent Mass Mailing #4 - Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-0687
EPA Comment ID: 20017
EPA Comment Code: 5300

Comment: All Americans deserve healthy and clean drinking water. The EPA should not finalize this decision until the scientific review is complete and should make decisions that are consistent with the agency's own scientists. Contrary to your claims, protecting the health of young children is indeed a "meaningful opportunity for health risk reduction."

Response: See response to comment code 5300.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0776
EPA Comment ID: 20186
EPA Comment Code: 5300

Comment: * a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Response: See response to comment code 5300.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-0671
EPA Comment ID: 20245
EPA Comment Code: 5300

Comment: Perchlorate is found in drinking water in 35 states, and according to the EPAâ€™s own data, 16 million Americans are at risk of being exposed to this dangerous chemical. Setting a standard for perchlorate will absolutely present â€˜a meaningful opportunity for health risk reduction.â€™

Response: See response to comment code 5300.

Commenter Name: Ed Thomas
Commenter Organization: National Rural Water Association (NRWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0163
EPA Comment ID: 20272
EPA Comment Code: 5300

Comment: Second, Rubin, etal (see reference 2 electronic attachment - "Rubin trade off health risk final.pdf") [see PDF of docket ID EPA-HQ- OW-2007-0068-0163] have documented quantitative evidence that when regulatory costs increase in the order of $25 per month, significant numbers of customers are forced into spending choices that have health outcomes that may outweigh the projected benefits of the regulation. NRWA strongly feels that when evaluating whether a regulation will result in a meaningful health benefit, EPA must take these effects into consideration. This is essentially an affordability issue and NRWA recommends that EPA include appropriate affordability criteria in its CCL evaluation and its future determinations when regulating or not regulating perchlorate.

Response: EPA has determined that the following three SDWA criteria for regulatory determination have been met for perchlorate: (1) It has an adverse effect on the health of persons; (2) It is known to occur in public water systems with a frequency and at levels of public health concern; and (3) In the sole judgment of the Administrator, regulation of perchlorate presents a meaningful opportunity for health risk reduction for persons served by public water systems. . This action notifies interested parties of EPA's determination to regulate perchlorate, and thus imposes no requirements on public water systems. This action also initiates the process to develop a national primary drinking water regulation (NPDWR) for perchlorate. EPA will now begin developing a proposed NPDWR and Maximum Contaminant Level Goal (MCLG). EPA plans to publish the proposed NPDWR for public comment along with health risk reduction benefits, and cost analyses, feasibility analyses and other analyses required for regulatory development under the SDWA. In proposing an NPDWR the Administrator will also describe variance technology for perchlorate that the Administrator finds are available and affordable for public water systems of varying size, considering the quality of the source water to be treated.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group (PSG)
EPA Document ID: EPA-HQ-OW-2007-0068-0168
EPA Comment ID: 20282
EPA Comment Code: 5300

Comment: EVALUATION OF POTENTIAL HEALTH EFFECTS ALONG WITH OCCURRENCE AND EXPOSURE RESULTS REVEALS THAT REGULATION OF PERCHLORATE WOULD NOT PRESENT A MEANINGFUL OPPORTUNITY FOR RISK REDUCTION

EPA establishes the HRL based on the RfD and the RSC and then compares the occurrence data to the health benchmark. Assuming an RSC of one (which yields an HRL of 24.5 ppb drinking water equivalent), the population exposed to perchlorate in drinking water above EPA's evaluative criteria - ½ and 1 times the health benchmark - are small fractions of the total population served by public drinking water systems. The populations exposed to perchlorate above these benchmarks is lower than the populations for other chemicals for which EPA has determined a drinking water standard would not reduce risk in a meaningful manner.

A comparison of occurrence data for perchlorate and relevant compounds from EPA's CCL 1 regulatory determinations and CCL2 proposed determinations reveals that perchlorate ranks as a lower opportunity for risk reduction than sodium, manganese, sulfate, and boron, all four of which EPA has made or proposed determinations not to regulate.

Further explanation of our evaluation of the third statutory criteria for meaningful opportunity for risk reduction is contained in Attachment 4 [See PDF of docket ID EPA-HQ-OW-2007-0068-0168].

Response: See response to comment ID 21028 under comment code 5200.

Commenter Name: Melanie A. Marty, Ph.D.
Commenter Organization: Children's Health Protection Advisory Committee
EPA Document ID: EPA-HQ-OW-2008-0692-0962
EPA Comment ID: 20423
EPA Comment Code: 5300

Comment: The third condition of the SDWA, that the Agency has a meaningful opportunity for health risk reduction, is also met for perchlorate. The setting of an MCL will trigger requirements for testing to determine whether there are exceedances, and fortunately, sensitive test methods and effective treatment systems are readily available. Therefore, the Administrator has the opportunity to intervene to protect the health of millions of pregnant women and their fetuses, and lactating women and infants across the country who would otherwise be exposed to unsafe levels of perchlorate.

Response: See response to comment code 5300.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection
EPA Document ID: EPA-HQ-OW-2008-0692-1422
EPA Comment ID: 20434
EPA Comment Code: 5300

Comment: 9. MassDEP Believes That a National Perchlorate Drinking Water Standard Provides a Significant Risk Reduction Opportunity. Table 2 of the Federal Register publication

provides information on the occurrence and population estimates for perchlorate above various thresholds. The table shows that up to 2.0 million people would be provided drinking water above 15 ppb, a value that, based on EPA's own estimates, is not protective of the breast or bottle fed infant, yet which is EPA's proposed HRL. EPA does not explain in the Federal Register how it reached its conclusion that protecting up to 2.0 million people is not a meaningful opportunity for risk reduction for persons, in particular infants, served by public water systems.

Response: EPA has determined that perchlorate meets the criteria for regulating a contaminant in Section 1412(b)(1)(A) of SDWA. As previously discussed in the Federal Register Notice, perchlorate may have an adverse effect on the health of persons and perchlorate is known to occur or there is a substantial likelihood that perchlorate will occur in public water systems with a frequency and at levels of public health concern. Moreover, in light of the discussion in this notice and the information available at this time, the Administrator finds that regulation of perchlorate in drinking water systems presents a meaningful opportunity for health risk reduction for persons served by public water systems. Therefore, EPA will initiate the process of proposing a NPDWR for perchlorate. See response to comment code 6120 and 5220.
See response to comment code 5220.

Commenter Name: J. Green
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0148
EPA Comment ID: 20462
EPA Comment Code: 5300

Comment: Setting a standard for perchlorate will absolutely present 'a meaningful opportunity for health risk reduction.' I urge you to do so in accordance with the Safe Drinking Water Act and protect Americans' health.

Response: See response to comment code 5300.

Commenter Name: Raimonde
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1513
EPA Comment ID: 20502
EPA Comment Code: 5300

Comment: With respect to EPA-HQ-OW-2008-0068:

It is recognized that this issue has been a difficult one and much work on behalf of EPA with it's extensive resources and interest groups, the dominant ones also possessing significant resources. However, EPA's proposal to avoid regulation fails to meet the Agency's overarching mandate to protect human health and the environment. We know of specific cases where in fact perchlorate exposure has affected public health and in those cases, there is little choice but for the public to consume a basic resource made available by their communities or their other limited means of water supply.

Although considering the argument regarding significance of the percentage of water supplies affected accounting for a small percentage, EPA has inproperly weighted its importance. What it has thus done, is use a predjudiced method to arrive at a conclusion that by regulating perchlorate, it would have no material effect on improving human health. This is clearly incorrect as the data reviewed by the wider scientific community has concluded that there are negative health effects resulting from exposure, some of them quite serious. We further know through no small body of evidence that regulating contaminants has demonstrated, without question, the improvement on public health. By arbitrarily setting the criteria at some percentage affected is contrary to sound public health protection and contrary to the public's expectation for EPA.

For EPA to conclude based on the guidance criteria interpreted narrowly to mean that some percentage of affected are not significant is plainly contrary to the principles of the mandate to protect human health and the environment.

I encourage the Agency to reconsider this matter and set a national standard.

Response: See response to comment code 5300.

Commenter Name: Thomas L. Schoaf
Commenter Organization: Cities of Litchfield Park and Goodyear, AZ
EPA Document ID: EPA-HQ-OW-2008-0692-1552
EPA Comment ID: 20520
EPA Comment Code: 5300

Comment: Given that the first two SDWA criteria have been met, and that there are available technologies to treat perchlorate, we believe that the third and final criterion has also been met and that a national standard set by the EPA presents a meaningful and appropriate risk reduction opportunity.

Further, a national standard is necessary to avoid a patchwork of potentially conflicting regulations amongst the various states . This is even more critical given that many states share water resources (such as the Colorado River water shared by Arizona and six other western states).

Therefore, we, the undersigned, request that the EPA reconsider its determination and establish a national maximum contaminant level for perchlorate

Respectfully,

Thomas L. Schoaf, Mayor City of Litchfield Park

James Cavanaugh, Mayor City of Goodyear

cc: Senator John McCain Senator Jon Kyl Congressman Trent Franks Senator Robert Blendu Representative John Nelson Representative Jerry Weiers Councilmembers, City of Goodyear Councilmembers, City of Litchfield Park

Water Docket, Docket ID No. EPA-HQ-OW-2008-0068 Environmental Protection Agency Mailcode : 2822T, 1200 Pennsylvania Ave., NW, Washington, DC 20460

Mary Aycock U.S. Environmental Protection Agency Region IX 75 Hawthorne Street SFD-8-2 San Francisco, CA 94105-3901

Cathy O'Connell Arizona Department of Environmental Quality 1110 W. Washington Street Phoenix, AZ 85007

Response: See response to comment code 5300.

Commenter Name: Jimmy Spearow
Commenter Organization: Sacramento Chapter, Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-1672
EPA Comment ID: 20590
EPA Comment Code: 5300

Comment: The data show that not regulating this harmful chemical in our drinking water is unacceptable. We disagree with the EPA statment that a national standard for perchlorate "would not present 'a meaningful opportunity for health risk reduction.'" Setting a standard for perchlorate will absolutely present 'a meaningful opportunity for health risk reduction.'

Response: See response to comment code 5300.

Commenter Name: Ed Thomas
Commenter Organization: National Rural Water Association
EPA Document ID: EPA-HQ-OW-2008-0692-1669
EPA Comment ID: 20620
EPA Comment Code: 5300

Comment: Rubin, etal (see reference 1 electronic attachment - "Rubin trade off health risk final.pdf") [See PDF Docket ID EPA-HQ-OW-2008-0692-1669] have documented quantitative evidence that when regulatory costs increase in the order of $25 per month, significant numbers of customers are forced into spending choices that have health outcomes that may outweigh the projected benefits of the regulation. NRWA strongly feels that when evaluating whether a regulation will result in a meaningful health benefit, EPA must take these effects into consideration. This is essentially an affordability issue and NRWA recommends that EPA include appropriate affordability criteria in its final determination to not regulate perchlorate.

Response: See response to comment code 5300, comment ID 20272.

Commenter Name: Robert Howd
Commenter Organization: California Environmental Protection Agency, Water Toxicology Section
EPA Document ID: EPA-HQ-OW-2008-0692-1671
EPA Comment ID: 20651
EPA Comment Code: 5300

Comment: IV (C), p 60280. A meaningful opportunity for health risk reduction. When drinking water consumption estimates that are protective of the exposed population are included in the

population exposure estimates, the number of people exposed to estimated excessive levels of perchlorate is markedly increased. When it is considered that the population at risk is not pregnant women, but their fetuses - and we all are fetuses once in our life - the population at risk balloons. Therefore it seems to us that the opportunity for a meaningful health risk reduction has been greatly understated.

Response: See response to comment code 5300.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1748
EPA Comment ID: 20655
EPA Comment Code: 5300

Comment: Fourth, since the scientific literature on perchlorate is extensive, EPA can rely on multiple approaches to determine that there would not be a meaningful opportunity for risk reduction through a national drinking water standard. As the PSG has stated in its public comments to EPA's May 1, 2007 notice (see attached)[No attachement provided], EPA reached its conclusions through several approaches, all with ample scientific justification. The literature on human health effects from perchlorate consists mainly of clinical, occupational, or ecological studies. There are also some well designed animal studies that have contributed to the health effects database. As EPA has stated repeatedly, PBPK modeling allows the agency to give policy officials more scientific support for interspecies and intraspecies uncertainty factors. Following EPA's first draft risk assessment for perchlorate in 1998, Dr. Curtis Klaassen, the Chair of the external peer review panel stated, "...a predictive risk assessment for perchlorate is possible and should be pursued in the next iteration of this assessment."[FN7: Curtis Klaassen, US EPA Perchlorate Peer Review Workshop, 1999.] EPA's consideration of its findings in its preliminary determination is exactly the use of compelling scientific information to support its policy decisions your November 5th letter [See PDF Docket ID EPA-HQ-OW-2008-0692-1749] endorses.

Response: No response necessary for this comment.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1748
EPA Comment ID: 20657
EPA Comment Code: 5300

Comment: While determining a "meaningful opportunity for risk reduction" is appropriately a policy decision it must be based on the best available scientific data. The best available data on perchlorate exposure suggest that very few individuals will be exposed to a dose of perchlorate greater than the RfD by drinking water with a perchlorate concentration above the HRL. Further, since the HRL is based on the NAS-recommended reference dose which is set at the no observed effect level (NOEL), which the NAS panel noted is a more conservative and health protective approach than using EPA's traditional approach of relying on the no observed adverse effect level (NOAEL)[FN9: NAS at 169, (pdf version).], along with an additional safety factor applied to it, the quantifiable incremental risk would appear to be very small.

Response: See response to comment code 5200. Regarding the comment about exposures above the RfD, the data underlying the definition of iodide uptake inhibition as a precursor effect and its relationship to the continuum of adverse thyroid outcomes reflects an understanding of effects in adults. The relationship of the precursor event to the adverse outcome in children has not been studied. Thyroid hormone status in neonates and infants is much less resilient than in adults. Generally speaking, they do not have iodide stores sufficient to offset the effects of reduced iodide uptake. Half-lives for circulating hormones are shorter than for adults, making infants and neonates less able to maintain stable hormone levels in the face of a chemical insult. The less resilient infant and neonatal system makes the exposure gap between a precursor event (iodide uptake inhibition due to perchlorate) and an adverse effect (reduced T3/T4 levels) much narrower than for adults. The distinction between the two may be blurred for the very young.

Commenter Name: Lyndsey Crum
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1732
EPA Comment ID: 20678
EPA Comment Code: 5300

Comment: November 10, 2008

Eric Burneson Office of Ground Water and Drinking Water Standards and Risk Management Division Environmental Protection Agency

RE: [EPA-HQ-OW-2008-0068; FRL-8727-6] Drinking Water: Preliminary Regulation Determination on Perchlorate

The agency should adopt its determination not to enact a NPDWR for perchlorate on the basis of the authority to promulgate NPDWR under the Safe Drinking Water Act.

The agency's notice indicates that SDWA requires EPA to promulgate an NPDWR for a contaminate if three conditioned are identified: (a) The contaminate may have an adverse effect on the health of persons; (b) the contaminate is known to occur or there is a substantial likelihood that the containment will occur in public water systems with frequency and at levels of public health concern; and (c) in the sole judgment of the Administrator, regulation of such contaminate presents a meaningful opportunity for health risk reduction for persons served by public health water systems.

The research presented and previous comments do not clearly establish condition two, and by construction, condition three. Therefore EPA is not required to regulate perchlorate in public water systems.

Response: See response to comment code 5300.

Commenter Name: Heather Hesse-Stromberg
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1763
EPA Comment ID: 20697
EPA Comment Code: 5300

Comment: Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought. A national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Response: See response to comment code 5300.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1983
EPA Comment ID: 20820
EPA Comment Code: 5300

Comment: The EPA is not accurate in determining that NPDWR for perchlorate would "not present a meaningful opportunity for health risk reduction for persons served by public water systems."

Response: See response to comment code 5300.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20897
EPA Comment Code: 5300

Comment: November 11, 2008

U.S. Environmental Protection Agency Water Docket EPA Docket Center 1200 Pennsylvania Avenue, NW Washington, DC 20460

Letter to EPA re: Preliminary Regulatory Determination on Perchlorate (Docket ID No. EPA-HQ-OW-2008-0692)

Dear Administrator Johnson:

Environmental Working Group (EWG) strongly disagrees with EPA's recent finding that setting a national drinking water standard for perchlorate would not present "a meaningful opportunity for health risk reduction for persons served by public water systems" (EPA 2008). The science provides overwhelming evidence that the tens of millions of people drinking perchlorate in tap water face real health risks that only EPA can protect them from. But the agency has chosen not to act and by failing to act, EPA has sacrificed its scientific integrity.

Response: See response to comment code 5300.

Commenter Name: Ron Curry
Commenter Organization: New Mexico Environment Department
EPA Document ID: EPA-HQ-OW-2008-0692-1796
EPA Comment ID: 20938

EPA Comment Code: 5300

Comment: As to the third criterion, EPA concludes that a national primary drinking water regulation for perchlorate would not present a meaningful opportunity to reduce health risks for persons served by public water systems.[FN25: 73 Fed. Reg. at 60280.] EPA bases this conclusion on the flawed analysis, described above, in which the agency determined that perchlorate occurs only infrequently at levels of public health concern. EPA reiterated that of the 900,000 to two million people who may be ingesting public drinking water at levels above the HRL of 15 ug/L, "fewer than 30,000 of them are pregnant women at any given time."[FN26: Id.] EPA's conclusion fails to account for the reduced health risks to pregnant women in the future, and to their fetuses; to infants; and to persons with thyroid disorders.

Response: EPA believes that regulating perchlorate in drinking water presents a meaningful opportunity for health risk reduction and has decided to regulate perchlorate in drinking water. See response to comment code 6120.

EPA has made this determination based on a consideration of the best available peer reviewed science and data collected in accordance with accepted methods related to perchlorate occurrence in drinking water, the presence of perchlorate in foods, and the potential health effects of exposure to perchlorate.

EPA has determined that perchlorate meets the criteria for regulating a contaminant in Section 1412(b)(1)(A) of SDWA. As previously discussed in the Federal Register Notice, perchlorate may have an adverse effect on the health of persons and perchlorate is known to occur or there is a substantial likelihood that perchlorate will occur in public water systems with a frequency and at levels of public health concern. EPA believes that the UCMR 1 is the best available data on the frequency and level of perchlorate occurrence in public water systems nationally. UCMR 1 indicated that 5.1 to 16.6 million people are served by PWSs, for which we have data, that have detected perchlorate above the minimum reporting level. In light of the discussion in this notice and the information available at this time, the Administrator finds that regulation of perchlorate in drinking water systems presents a meaningful opportunity for health risk reduction for persons served by public water systems. Therefore, EPA will initiate the process of proposing a NPDWR for perchlorate. See response to comment code 6120 and 5220.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20981
EPA Comment Code: 5300

Comment: The U.S. population is about 300 million people with about 6.8%, or 20 million, under 5 years old. On average, therefore, there are about 4 million kids in each year of life (from zero to five). With 4 million kids under 1 year old, including infants, there are 400,000 in the 90th percentile of water consumers, meaning that at the proposed HRL, these 400,000 would have a perchlorate intake, each day for their whole first year of life, that exceeds the reference dose. EPA's proposed model shows that there are 400,000 children under the age of 1 who would exceed the daily reference dose and this is likely underestimate of the highly exposed. Thus, the evidentiary record

does not support EPA's proposed determination. Rather, the evidentiary record makes clear that regulating these exposures does represent "a meaningful opportunity for health risk reduction for persons served by public water systems."

Response: See response to comment codes 5200 and 5300.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 21000
EPA Comment Code: 5300

Comment: The U.S. population is about 300 million people.[FN55: U.S. Census Bureau quick facts. 2006. http://quickfacts.census.gov/qfd/states/00000.html] Of the total, about 6.8%, or 20 million, are under 5 years old, an average of about 4 million kids of each year of life. This is a reasonable estimate supported by the fact that there were about 4,329,000 live births in the U.S. in 2007.[FN56: National Vital Statistics Reports, Vol 57, No 5. http://www.cdc.gov/nchs/data/nvsr/nvsr57/nvsr57_05.htm] If there are 4 million children less than 1 year old, including infants, then 400,000 of them would be in the 90th percentile of water consumers. This means that at the proposed HRL, 400,000 children and infants will exceed the reference dose for perchlorate every day for their entire first year of life.

As part of its basis for the preliminary determination not to regulate perchlorate because it does not feel there is a meaningful opportunity to reduce health risks, EPA acknowledged that perchlorate could have an adverse effect on human health.[FN57: 73 Fed. Ref. at 60275.]

Furthermore, EPA's own staff experts have provided data to show that at the HRL, 400,000 infants and children would consume perchlorate on a daily basis that exceeded the reference dose. Rather, EPA states that 30,000 pregnant women would be exposed to these levels of perchlorate, and that number does not provide a meaningful opportunity to reduce health risks. While we take issue with EPA's determination that reducing the exposure of 30,000 pregnant women to perchlorate is not meaningful, EPA must explain why reducing the exposure of 400,000 children and infants to perchlorate is not a meaningful opportunity to reduce health risks.

Response: See response to comment codes 5200 and 5300.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 21005
EPA Comment Code: 5300

Comment: Second, even without those peer review comments, existing data on perchlorate exposure and effects, especially on vulnerable subpopulations, demonstrates that setting a national primary drinking water standard for perchlorate would provide a meaningful opportunity for health risk reduction. EPA is therefore required to set such a standard under the Safe Drinking Water Act.

Response: See response to comment code 5300.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-2082
EPA Comment ID: 21029
EPA Comment Code: 5300

Comment: 12. Finally, your letter argues that the "meaningful opportunity for risk reduction" criterion is met because an MCL will trigger testing for exceedances.

While determining a meaningful opportunity for risk reduction is appropriately a policy decision it must be based on the best available scientific data. The best available data on perchlorate exposure suggest that very few individuals will be exposed to a dose of perchlorate continuously for years greater than the RfD by drinking water with a perchlorate concentration above the HRL. Further, since the HRL is based on the NAS-recommended RfD which is set at the NOEL, which the NAS panel noted is a more conservative and health protective approach than using EPA's traditional approach of relying on the no observed adverse effect level (NOAEL) [FN10: NAS at 169, (pdf version).], along with an additional safety factor applied to it, the quantifiable incremental risk would appear to be small.

I hope you find these comments helpful; we would be happy to talk further with you about this important issue. Further, if the CHPAC opts to convene a public meeting on perchlorate, the PSG would welcome an opportunity to present the scientific literature and our public comments. For your convenience, we have included those comments for your review. Our comments review the science of perchlorate beginning with the comprehensive NAS review followed by subsequent studies and then apply them in the statutory and policy framework in which EPA has made its preliminary determination. Thank you for your time and attention.

Sincerely, Michael Girard Chairman, Perchlorate Study Group cc: Marcus Peacock, Deputy Administrator Benjamin Grumbles, Assistant Administrator, Office of Water Cynthia Dougherty, Director, Office of Ground Water and Drinking Water Eric Burneson, Chief, Targeting and Analysis Branch

Response: See response to comment ID 20657 under comment code 5300.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21090
EPA Comment Code: 5300

Comment: Public water systems do not offer a meaningful risk reduction opportunity since EPA's data show that only a few percent of systems have had detectable levels of perchlorate and virtually all of them are routinely below EPA's unusually protective reference dose (RfD). EPA also has extensive data that show the US population's total exposure to perchlorate - from food and water - is below the RfD for 99.996 percent of the population. EPA should spend its limited resources on significant potential threats to human health in order to most effectively protect the public health.

The comments below present a detailed analysis of the issues relating to EPA's determination. The attachment from Intertox describes in more detail the state of the scientific literature. The overwhelming weight of scientific evidence indicates that EPA is acting correctly in its determination not to establish a Federal drinking water standard.

Response: See response to comment code 5200.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21097
EPA Comment Code: 5300

Comment: IV. The Scientific Literature Supports EPA's Findings that There is Not a Meaningful Opportunity for Risk Reduction from a National Drinking Water Standard

The evaluation of data on the health effects of perchlorate, national occurrence, and exposure using the SDWA "meaningful risk reduction" criteria support EPA's determination that an NPDWR for perchlorate is unnecessary.

Following the release of the NAS report, EPA set an RfD for perchlorate at 0.7 ug/kg-d. The RfD is defined as "...an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime (EPA, 2005). The RfD does not distinguish between perchlorate in drinking water and in food. In establishing the amount of perchlorate that would be expected to pose no risk to health in drinking water alone, the RSC is factored in resulting in the HRL or "the benchmark against which EPA compared the concentration of a contaminant found in public water systems to determine if it is at a level of public health concern (73 FR 60275)." EPA has established that it would not be meaningful to set an NPDWR, but is now considering issuing a Health Advisory (HA), in the form of an MCLG.

If EPA decides a Health Advisory is necessary, the RfD is sufficiently conservative to serve as the HA. As presented in the PSG's comments on the May 1, 2007 notice, the best available scientific analysis demonstrates that all of EPA's approaches lead to an RSC of essentially one. Drinking water is not a meaningful contributor to total perchlorate exposure - and not even a minor source of total inhibition of iodine uptake, the non-adverse effect that is the basis of the RfD.

Alternatively, the HRL identified in its preliminary determination could also serve as an even more conservative, but no more protective, HA. What is striking is that either approach would be highly conservative. In fact, the high level of conservatism, and health protection, is far greater than EPA indicated by the agency's longstanding policies, themselves properly weighted toward greater protection.

The HRL relies on the NAS-recommended RfD that has several levels of conservatism (that is, exceptional health protection) built into calculation of dose. As EPA has noted, its RfD was based upon the recommendations of the NAS which, as noted, used a much more conservative and health-protective approach to derive its recommended safe dose than EPA has previously used.[FN3: NAS, at 170-71.] EPA embeds an additional level of conservatism in calculating the final

HRL by verifying their calculations using PBPK modeling of pregnant women as opposed to relying on the standard of assuming an adult as the focus of its calculations.

To determine the RSC, the EPA uses the NHANES-UCMR data to estimate doses to people who were exposed through food only (73 FR 60273). The UCMR 1 shows the median concentration of perchlorate in drinking water to be 6.4 ug/L (73 FR 60269). The 90th percentile estimated dose to the women exposed only through food was 0.263 ug/kg/d which corresponds to 38% of the RfD. This leaves 62% of the RfD left for exposure through water. Using this data, a HRL was calculated as such:

HRL = (RfD x BW / DWI) x RSC Where, RfD = 0.7 mg/kg-d BW = 70 kg DWI = drinking water intake = 2 L/d RSC = 62%

This results in a HRL of 15 ppb. The derivation of the HRL was based on the body weight and water intake of an adult[FN4: The standard EPA default procedure for converting dose into drinking water equivalent levels assumes 2 liters (67.6 oz) of water consumed per day and a body weight of 70 kg (154 lbs). These default values are not symmetrically representative of the population. This water consumption (WC) default is approximately equal to the 88th percentile water intake for adults aged 20 through 64 (calculated from Table 3-11 of U.S. EPA's Exposure Factors Handbook; EPA, 1999). However, the default body weight of 70 kg is approximately equal to the 27th percentile of the distribution for adult males aged 18-74 and the 70th percentile of the distribution for adult females (from EPA, 1999; Tables 7-3 and 7-4).], not the pregnant woman and her fetus. The EPA modeled the amount of IUI in a pregnant woman and her fetus using PBPK modeling and found that the amount of IUI expected was equivalent to the NOEL from Greer et al. (2002). EPA then compares this HRL to perchlorate occurrence data in drinking water to evaluate the percent of the population exposed to perchlorate above the HRL.

For the perchlorate determination, EPA may also use the evaluation criteria under the CCL 1 regulatory determinations to determine whether a meaningful opportunity to regulate health risk exists. EPA's regulatory evaluation process follows the recommendations on a protocol from EPA's stakeholder advisory panel, the National Drinking Water Advisory Council (NDWAC). To assist EPA in evaluating the third statutory criteria, the NDWAC protocol recommended "that EPA consider estimating the national population exposed above half the health reference level (or benchmark) and the national population exposed above the health reference level (or benchmark)."

EPA used this approach for evaluating substances in its CCL 1 regulatory determinations. This approach allows EPA's decision-making process to be replicated and therefore provides greater transparency and objectivity into the agency's final decisions rendered on the third statutory criterion. It also has the support of major stakeholders and has been subject to public comment. The PSG points out that EPA could, in addition to its valid reasoning in the preliminary determination, relay a similar evaluation process for its perchlorate determination.

A comparison of occurrence data for perchlorate and relevant compounds from EPA's CCL 1 regulatory determinations and the CCL 2 determinations reveals that perchlorate ranks as a lower opportunity for risk reduction than the sodium, manganese, sulfate, and boron, all of four of which EPA has made determinations not to regulate.

If the HRL is 15 ppb, EPA estimates that between 0.29 percent and 0.8 percent of PWSs have at least one detection greater than 15 ug/L, affecting 0.9 million to 2 million people served. Between 1.14 percent and 2.12 percent of PWSs had at least one detect with concentrations at 1/2 of the HRL (7 ug/L), affecting between 0.8 percent and 2.5 percent of the population served or between 2.2 million and 7.2 million people served, respectively.

[Table 1: Comparison of Risk Opportunity between Perchlorate and Other Compounds - See PDF Docket ID EPA-HQ-OW-2008-0692-1855]

The percentage of PWSs with perchlorate detections was very low (3.6 percent) compared to the next lowest unregulated compound, manganese at 68 percent. Sodium, for example, was detected in all PWSs. Perchlorate also has one of the lowest populations served by PWSs with detections above half the HRL with 2.2 million people. Perchlorate is well within the range of values for the evaluation criterion EPA uses. Like these other constituents, perchlorate is widely found in the diet and has minimal adverse health effects at the RfD. Although EPA's approach of using actual food data has more scientific justification, even if EPA adopts its customary approach for the proposed regulatory determination, it should find that perchlorate does not pose a meaningful opportunity to reduce risk.

Response: See response to comment codes 5300 and 5200. EPA considered national occurrence and the severity of health effects from perchlorate and concluded that regulation was warranted, so EPA has determined that perchlorate should be subject to an NPDWR. The Agency plans to prepare and make available a regulatory health effects support document as part of its regulatory promulgation process. If an NPDWR is promulgated a health advisory will be unnecessary. EPA agrees with the commenter that the RfD is conservative and protective of health.
Regarding the PBPK model, after further consideration of the peer review and public comments, EPA concludes that the PBPK modeling analysis, in the context of the perchlorate regulatory determination, is useful in examining which life stages are most susceptible to the effects of perchlorate. For example, the model indicates that a fetus may be seven times more sensitive to the effects of perchlorate than a pregnant woman. The model also allows for the estimation of the concentration of perchlorate in breast milk (thus breast-fed infant exposure) at various maternal perchlorate exposure levels. However, because of the stated limitations, EPA has decided the model does not directly bear on the current decision regarding the need for a NPDWR for perchlorate. EPA is continuing to evaluate whether the model could be used in setting a NPDWR for perchlorate. Regarding the suggestion to compare the risk opportunity from detects in public water systems between perchlorate and other compounds that EPA has decided not to regulate, EPA does not believe it's appropriate to factor these comparisons into the decision whether to regulate a contaminant. The Administrator will make these determinations on a case-by-case, contaminant specific basis. In making a regulatory determination, the Administrator considers the adverse health effect of the particular contaminant at issue as well as the occurrence or likelihood of occurrence of the contaminant in public water systems with a frequency and at levels of public health concern. In addition, even if such comparisons were appropriate, the occurrence level of perchlorate at the levels of public concern identified by EPA are higher than most of the contaminants for which EPA has made a negative determination. Finally, it is the sole judgment of EPA's Administrator to determine whether there is a meaningful opportunity to reduce health risk for persons served by public water systems.

Commenter Name: Tigris Powers

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2244
EPA Comment ID: 22427
EPA Comment Code: 5300

Comment: All Americans deserve healthy and clean drinking water. The EPA should not finalize this decision until the scientific review is complete and should make decisions that are consistent with the agency's own scientists. Contrary to your claims, protecting the health of young children is indeed a "meaningful opportunity for health risk reduction."

Sincerely, Tigris Powers 2421 Topanga Skyline Drive Topanga, CA 90290

Response: See response to comment code 5300.

Commenter Name: Kraig Erickson
Commenter Organization: RMC Water and Environment (RMC)
EPA Document ID: EPA-HQ-OW-2008-0692-2299
EPA Comment ID: 24979
EPA Comment Code: 5300

Comment: All Americans deserve healthy and clean drinking water. The EPA should not finalize this decision until the scientific review is complete and should make decisions that are consistent with the agency's own scientists. Contrary to your claims, protecting the health of young children is indeed a "meaningful opportunity for health risk reduction."

Again, I urge you to reverse your decision and to set a national drinking water standard for perchlorate.

Response: See response to comment code 5300.

Commenter Name: Ed Thomas
Commenter Organization: National Rural Water Association (NRWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0521
EPA Comment ID: 28476
EPA Comment Code: 5300

Comment: In this time of severe economic stress in our society, it is particularly important that the benefits of a regulation be carefully weighed against the costs and only those with an overriding benefit/cost advantage be promulgated. For perchlorate it is clear that this advantage does not exist uniformly and in fact, for some communities the aforementioned reference provides evidence that the adverse health effects caused by the cost of the regulation may equal or outweigh the projected benefits.

Rubin, etal (see reference 1 electronic attachment - "Rubin trade off health risk final.pdf") have documented quantitative evidence that when regulatory costs increase in the order of $25 per month, significant numbers of customers are forced into spending choices that have health outcomes that may outweigh the projected benefits of the regulation. NRWA strongly feels that when evaluating whether a regulation will result in a meaningful health benefit, EPA must take these

effects into consideration. This is essentially an affordability issue and NRWA recommends that EPA include appropriate affordability criteria in its final determination to not regulate perchlorate.

Response: See response to comment ID 20272 under comment code 5300.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28874
EPA Comment Code: 5300

Comment: c) The SDWA requires that the regulation of such contaminants must present a meaningful opportunity for health risk reduction for persons served by public water systems. For perchlorate, no possible health benefit can occur when estimated exposure levels are below the NOEL for a nonadverse effect. Further, EPA adjusted the NOEL ten-fold lower to derive the RfD to account for sensitive subpopulations.

Response: See reponse to comment code 5200, comment ID 21028.

Commenter Name: Danielle Blacet
Commenter Organization: Association of California Water Agencies
EPA Document ID: EPA-HQ-OW-2009-0297-0208
EPA Comment ID: 28922
EPA Comment Code: 5300

Comment: 4) ACWA believes that the maximum contaminant levels (MCLs) established in Massachusetts and California have significantly reduced the current public exposure to perchlorate in drinking water. ACWA feels this has had an impact on the meaningful opportunity for health risk reduction that is available through a national drinking water standard for perchlorate.

Response: EPA acknowledges that there may be sources that had detected perchlorate from UCMR1 monitoring are either no longer being used or are being treated per the requirements of maximum contaminant levels established in California and Massachusetts; however, the 1996 amendments to the Safe Drinking Water Act require the Agency to consider the best available, peer reviewed science when developing drinking water standards. In applying these principles, "best available" usually refers to the availability at the time an assessment is made. See response to comment code 5300.

Commenter Name: Lucy Allen
Commenter Organization: Pacific Institute
EPA Document ID: EPA-HQ-OW-2008-0692-1770
EPA Comment ID: 29099
EPA Comment Code: 5300

Comment: We understand the need to balance costs and benefits in drinking water regulations, however, costs associated with the regulation of perchlorate will ostensibly be low, except in those cases where high levels of perchlorate exist and drinking water must be treated. For other systems, costs can be limited to periodic monitoring (e.g., once in every 4 years, as is done with

radionuclides). The cost of regulating perchlorate in our country's public drinking water, when compared with the myriad potential health-related costs, including added pressure on public health care systems, missed work and school days due to sickness, etc., may very likely prove the most cost-effective option.

In light of these concerns we sincerely hope that the EPA reevaluates its Preliminary Decision, taking into account the impact of this regulation on all vulnerable populations, the potential for remediation efforts, and the potential future contamination of drinking water. In addition, we hope that the agency fulfills its duty to protect the public health of the thousands of individuals who are affected by unsafe perchlorate exposure through public drinking water.

Sincerely, Lucy Allen Research Analyst Pacific Institute

Courtney Smith Research Analyst Pacific Institute

Response: Regarding the costs associated with regulating perchlorate, see response to comment ID 20272 under comment code 5300. Regarding EPA reevaluating its preliminary decision, see response to comment code 5300.

EPA Comment Code: 6000 EPA Actions

Individual Comments
Commenter Name: Stephen Haterius
Commenter Organization: The National Association of State Departments of Agriculture (NASDA)
EPA Document ID: EPA-HQ-OW-2009-0297-0500
EPA Comment ID: 28485
EPA Comment Code: 6000

Comment: The significance of this issue goes far beyond setting unwise regulatory precedent. An overly conservative perchlorate standard that is not based on sound, peer-reviewed science and an appropriate risk-based assessment could unintentionally lead to unjustified food scares on a wide variety of fresh fruits, vegetables, and dairy products. Food scares of this nature could where particular commodities are "black listed" without regard to science would have devastating economic impacts on agriculture producers and processors. Finally, the economic impacts associated with unfounded concerns over traces of perchlorate in food could lead to the relocation of agricultural production to countries that have food safety standards that are significantly lower than in the United States.

We appreciate your attention to our concerns and once again encourage you to extend the comment period for an additional 30 days.

Sincerely, Stephen Haterius Executive Director

Response: EPA believes that perchlorate meets the specific criteria for regulating a contaminant in Section 1412(b)(1)(A) of the Safe Drinking Water Act and therefore has determined that EPA should regulate perchlorate in drinking water. EPA discusses this conclusion in more detail in today's perchlorate Federal Register notice. EPA agrees that perchlorate is more widespread in foods than in public water systems, but EPA does not believe that the widespread presence of perchlorate in food overrides the opportunity for public health risk reduction for persons served by public water systems with perchlorate contamination. EPA's action considers the presence of perchlorate in food but would not impose regulatory requirements on perchlorate in food. Regulation of perchlorate in foods is outside the scope of this determination which is made under the authority found in the Safe Drinking Water Act, as amended in 1996.

EPA Comment Code: 6100 EPA's preliminary determination not to regulate perchlorate

Individual Comments
Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 28743
EPA Comment Code: 6100

Comment: September 16, 2009

U.S. Environmental Protection Agency Mailcode 2822T 1200 Pennsylvania Ave., NW. Washington, DC 20460

Subject: Docket ID No. EPA-HQ-OW-0297

Reference: Drinking Water: Perchlorate Supplemental Request for Comments (Federal Register / Vol. 74, No. 1591 Wednesday, August 19, 2009 / Notices

Attached, please find comments provided by the Nevada Division of Environmental Protection (NDEP) in response to the referenced "Supplemental Request for Comments" noticed by the U.S. Environmental Protection Agency (EPA) in the August 19, 2009 Federal Register; Docket ID No. EPA-HQ-OW-2009-0297. These comments are provided to assist the EPA in their efforts in evaluating whether there is a meaningful opportunity for human health risk reduction of perchlorate through a national primary drinking water rule.

The NDEP understands that in order to regulate a contaminant in drinking water [i.e., develop a maximum contaminant level (MCL)], EPA must determine that the contaminant meets the following three criteria:

1) The contaminant may have an adverse effect on human health;

2) The contaminant is known to occur (or there is a substantial likelihood that the contaminant will occur) in public water systems, with a frequency and at levels of public health concern; and

3) Regulation of such a contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems

The NDEP believes that the EPA cannot reliably demonstrate that all three criteria can be met (with respect to perchlorate) when all of the studies and available literature are used and new occurrence data are collected to inform the decision. Many studies have been conducted and the results peer reviewed and published since the National Academy of Science (NAS), National Research Center (NRC) provided their review in 2005. A number of these studies were conducted explicitly to fill data gaps present at that time. A thoughtful review of the entirety of the studies and literature, coupled with collection and analysis of up-to-date occurrence data, is recommended to allow EPA to meet its charge on this important decision.

Response: EPA has continued to review all the available data published concerning perchlorate in drinking water as it is made available. The regulatory determination made in today's Federal Register notice was based upon a consideration of the best available peer reviewed science and data, both recent as well as the information available and discussed in earlier Federal Register notices.

EPA Comment Code: 6110 Comments urging EPA not to regulate perchlorate

Response to Code 6110: After review of the available science, data and public comments, EPA has determined that perchlorate may have an adverse effect on the health of persons and that perchlorate is known to occur or there is a substantial likelihood it occurs in public water supply systems with frequency and at levels of public health concern. EPA has also determined that regulation of perchlorate presents a meaningful opportunity to reduce health risk for persons served by public water systems. The basis for EPA's determination is described in the Federal Register Notice for the final regulatory determination.

Individual Comments
Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group (PSG)
EPA Document ID: EPA-HQ-OW-2007-0068-0168
EPA Comment ID: 20278
EPA Comment Code: 6110

Comment: July 2, 2007

US Environmental Protection Agency Office of Water Docket (Mailcode 2822T) 1200 Pennsylvania Avenue, NW Washington, DC 20460

RE: Comments on Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List Rule Docket EPA-HQ-OW-2007-0068

The Perchlorate Study Group (PSG) is pleased to submit comments to EPA on Docket ID No. EPA-HQ-OW-2007-0068, entitled Drinking Water: Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List- Preliminary Determinations; Proposed Rule.[FN1: 72 Fed. Reg. 24015 (2007) (proposed May 1, 2007).]

The PSG is committed to ensuring that the best available science is made available in public debate and in the subsequent setting of regulatory standards.[FN2: In section 1412(b)(3)(A) of the 1996 Amendments to the Safe Drinking Water Act, Congress required EPA to use the best available science and data: "The Administrator shall use: (i) the best available, peer-reviewed science and supporting studies conducted in accordance with sound and objective scientific practices; and (ii) data collected by accepted methods or best available methods (if the reliability of the method and the nature of the decision justifies use of the data).] The member companies of the PSG include Aerojet, AMPAC, ATK, and Tronox.

The PSG has worked cooperatively and effectively with the US Environmental Protection Agency (EPA) and other federal agencies, state governments, water purveyors, and other business organizations to:

* increase scientific and medical understanding of perchlorate's possible effects on human health; and,

* assess the level of perchlorate in drinking water that will pose no cognitive risk.

In seeking public comment on its Second Contaminant Candidate List (CCL 2) Preliminary Determinations, EPA has expressed particular interest in receiving information regarding the adequacy of available occurrence and exposure data with respect to making a regulatory determination for perchlorate. In addition, EPA has asked for public input on scientific analysis options that would assist the Agency in reaching a regulatory determination for perchlorate.

The PSG members are manufacturers and users of perchlorate who are actively remediating areas of past releases, and are citizens concerned with the protection of the public's health. As such, the PSG member companies have a strong and unique commitment to ensuring that the best available science is applied in regulatory decision making.

Based on its thorough evaluation of the best available science, as well as consideration of the Agency's statutory authorities, the PSG respectfully submits:

* in light of the National Academy of Sciences comprehensive review, as well as numerous, peer-reviewed studies, the Agency has more than sufficient data on perchlorate's human health effects to make a regulatory determination for perchlorate on an expedited basis; and

* the extensive scientific record indicates that establishing a drinking water standard for perchlorate would not yield a meaningful opportunity to reduce risk to human health, as required under the Safe Drinking Water Act.

ANALYSIS AND OBSERVATIONS

EVALUATING THE 3 STATUTORY CRITERIA FOR THE REGULATORY DETERMINATION PROCESS

To determine whether to regulate a contaminant with a Federal drinking water standard, EPA evaluates three Safe Drinking Water Act criteria.[FN3: In section 1412(b)(1)(A) of the Safe Drinking Water Reauthorization Act of 1996, Congress established three criteria for use by EPA in making drinking water regulatory determinations: (i) the contaminant may have an adverse effect on the health of persons; (ii) the contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and, (iii) in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems. (See, 110 Stat. 1613, 1619; 42 USC. §300g-1(b)(1)(B)(ii)(II)).] EPA has determined that it must make an affirmative determination on all three criteria to move forward with regulation. If the Agency determines that a regulation is appropriate, EPA can make its regulatory determination for perchlorate in two ways:

1. through its longstanding approach used in the CCL 1 rulemaking and proposed for the CCL 2 determinations; or,

2. applying supplemental or alternative approaches reflecting new scientific information, using the uniquely conservative derivation of the perchlorate reference dose (RfD) for perchlorate, as well as the exceptionally deep and authoritative scientific literature on toxicity and population exposure.

No matter which approach EPA takes, the best available science runs inevitably to the conclusion that a perchlorate standard will not yield a meaningful opportunity to reduce risk to human health as required by the Safe Drinking Water Act.

EPA has more than sufficient data on perchlorate's human health effects as well as on occurrence and exposure to make a determination on perchlorate without delay. EPA is to be commended for its efforts to obtain public comment relating to the prospective use of supplemental or alternative approaches. These approaches are scientifically rigorous and upto- date, based on the peer- reviewed literature. Our collective goal of applying the best available science would point toward their use.

Nonetheless, should the agency elect to apply an approach based strictly on toxicology and modeled exposures, we anticipate it will yield the same conclusions, albeit, after a period of unnecessary delay.

Response: Please see the response to comment code 6110.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group (PSG)
EPA Document ID: EPA-HQ-OW-2007-0068-0168
EPA Comment ID: 20283
EPA Comment Code: 6110

Comment: CONCLUSION

In summary, EPA has an extraordinary wealth of comprehensive, authoritative scientific information relating to perchlorate's health effects, supplemented by extensive occurrence and exposure data. The Agency is therefore exceptionally well-positioned to issue a wellconsidered regulatory determination.

In this case, the Agency can rely on the scientific review by the NAS and its own subsequent analysis in setting a reference dose pursuant to the NAS Report. Subsequent, peer-reviewed studies provide additional information that corroborates the conclusions of the NAS and EPA.

The Agency can use its RfD as the HRL. EPA should take into account that the RfD is based on an unusually conservative point of departure, a NOEL (as opposed to the Agency's customary No Observed Adverse Effect Level), with an added safety factor of 10.

Ultimately, regardless of which approach EPA takes, the best available scientific data supports a determination that there is not a meaningful opportunity for risk reduction as required by the Safe Drinking Water Act.

The Perchlorate Study Group appreciates the opportunity to submit comments on this issue. If you have any questions regarding these comments, please do not hesitate to contact Michael Girard at (916) 355-2945.

Sincerely, Michael Girard The Perchlorate Study Group Attach:

[Attachment 1 - see PDF] [Attachment 2 - see PDF] [Attachment 3 - see PDF] [Attachment 4 - see PDF] [Attachment 5 - see PDF]

Response: Please see the response to comment code 6110. In light of the discussion presented in the final regulatory determination notice and the information available at this time, EPA expects to select an MCLG from among the range of potential alternative HRLs in the August 9, 2009 notice (74 FR 41883). These levels range from 1 μg/L to 47 μg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals in each life stage.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association
EPA Document ID: EPA-HQ-OW-2008-0692-1424
EPA Comment ID: 20437
EPA Comment Code: 6110

Comment: November 10, 2008 U.S. Environmental Protection Agency Office of Water Docket (Mailcode 2822T) 1200 Pennsylvania Ave. NW Washington, DC 20460

RE: Drinking Water: Preliminary Regulatory Determination on Perchlorate Docket EPA-HQ-OW-2008-0692

The American Water Works Association appreciates the opportunity to comment on the preliminary regulatory determination for perchlorate as detailed in the October 10, 2008 Federal Register notice (73 FR 60262). AWWA is an international, nonprofit, scientific and educational society dedicated to the improvement of drinking water quality and supply. Founded in 1881, the Association is the largest organization of water supply professionals in the world. Our 60,000 plus members represent the full spectrum of the drinking water community: treatment plant operators and managers, environmental advocates, engineers, scientists, academicians, and others who hold a genuine interest in water supply and public health. Our membership includes more than 4,700 utilities that supply roughly 80 percent of the nation's drinking water. Based on this broad membership base, these comments should be considered as representative of the drinking water community in general.

AWWA has always been a strong' advocate of the process established under Section 1412(b) of the 1996 SDWA Amendments to ensure that appropriate and scientifically based standards are developed and enforced by the Agency. The SDWA defined three (3) key criteria for identification of contaminants for potential regulation:

i.the contaminant may have an adverse effect on the health of persons;

ii.the contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and

iii.in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

Based on these SDWA criteria and currently available, AWWA supports EPA's proposed regulatory determination for perchlorate: Additionally, AWWA supports the EPA decision to issue a Health Advisory for perchlorate at the time of the final determination which provides important technical guidance to Federal agencies, State governments, and other public health officials.

The above conclusion is supported by independently developed assessments of both occurrence and exposure commissioned by AWWA. This research supports the finding that a national standard for perchlorate would not present a meaningful opportunity for health risk reduction for persons served by public water systems. The following provides a summary of our findings which are in the process of being submitted for peer-review.

Response: Please see the response to comment code 6110.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association
EPA Document ID: EPA-HQ-OW-2008-0692-1424
EPA Comment ID: 20442
EPA Comment Code: 6110

Comment: Conclusion

Based on our own analysis and related data presented in the proposed decision, AWWA believes that EPA's decision is supported by the criteria established in the SDWA. AWWA appreciates the opportunity to comment on these important drinking water issues. If you have any questions about these comments, please feel to call Kevin Morley or me in our Washington Office at 202-628-8303.

Yours Sincerely, Thomas W. Curtis Deputy Executive Director

cc: Benjamin Grumbles - USEPA OW Cynthia Dougherty - USEPA OGWDW Eric Burneson - USEPA OGWDW Brian Mannix - USEPA OPEI Alan Roberson Kevin Morley

References

Blount BC, Valentin-Blasini L, Osterloh JD, Mauldin JP, Pirkle JL. (2006) Perchlorate exposure of the U.S. population, 2001-2002. Journal of Exposure Science and Environmental Epidemiology 17(4):400-7.

Brandbuber, Phillip, Clark, Sarah and Morley, Kevin M. (pending publication in Journal AWWA). The Occurrence of Perchlorate in Public Drinking Water Systems.

Crawford-Brown, Doug, Raucher, Bob and Harrod, Megan. 2006. Inter- Subject Variability of Risk From Perchlorate in Community Water Supplies. Environmental Health Perspectives 114:7:975.

Mendez, William and Dederick, Elizabeth (2008). Estimating the Contribution of Drinking Water to Aggregate Perchlorate Intake of Reproductive Age Women in the U.S. Report prepared for the American Water Works Association, see enclosed Appendix A.

Appendix A: Estimating the Contribution of Drinking Water to Aggregate Perchlorate Intake of Reproductive Age Women in the U.S.

Response: Please see the response to comment code 6110.

Commenter Name: Colby Goodliffe
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1515
EPA Comment ID: 20504
EPA Comment Code: 6110

Comment: I recommend that EPA should not change its determination regarding the regulation of perchlorate. There is no need for every public water system in the US to test for a contaminant that only a few water sources contain. Let the states handle this on a case-by-case basis. I manage a public water system and we already spend thousands of dollars each year to test for contaminants that are not in our water and never have been in our water. I agree that we need to do as much as possible to ensure that our drinking water is safe, but the blanket regulations that govern drinking water are ineffective and facilitate wasteful spending of tax dollars.

Colby Goodliffe

Response: Please see the response to comment code 6110. The Agency analyzed occurrence data from the Unregulated Contaminant Monitoring Rule (UCMR), which is nationally representative, and found that perchlorate occurred in 26 states and 2 territories. Today's determination merely initiates the process of establishing a national primary drinking water regulation. It does not impose any requirements on public water systems. EPA will provide an opportunity to comment on the proposed regulation, along with health risk reduction and cost analysis, feasibility analysis, and other relevant analyses.

Commenter Name: Ed Thomas
Commenter Organization: National Rural Water Association
EPA Document ID: EPA-HQ-OW-2008-0692-1669
EPA Comment ID: 20617
EPA Comment Code: 6110

Comment: November 10, 2008

U.S. Environmental Protection Agency Office of Water Docket (Mailcode 2822T) 1200 Pennsylvania Ave. NW Washington, DC 20460

RE: Drinking Water: Preliminary Regulatory Determination on Perchlorate (Docket Number: EPA-HQ-OW-2008-0068)

To Whom It May Concern:

NRWA commends EPA for their proposed regulatory determination for perchlorate. We believe the Agency has relied on sound science and that a national standard for perchlorate would not result in a meaningful opportunity for health risk reduction.

Response: EPA believes that regulating perchlorate in drinking water presents a meaningful opportunity for health risk reduction. This determination is based on the best available peer reviewed science and data collected in accordance with accepted methods related to perchlorate's occurrence in drinking water, the presence of perchlorate in foods and the potential health effects of

exposure to perchlorate, and EPA's population exposure evaluation as described in more detail in the final regulatory determination.

Commenter Name: Ed Thomas
Commenter Organization: National Rural Water Association
EPA Document ID: EPA-HQ-OW-2008-0692-1669
EPA Comment ID: 20619
EPA Comment Code: 6110

Comment: In this time of severe economic stress in our society, it is particularly important that the benefits of a regulation be carefully weighed against the costs and only those with an overriding benefit/cost advantage be promulgated. For perchlorate it is clear that this advantage does not exist uniformly and in fact, for some communities the aforementioned reference provides evidence that the adverse health effects caused by the cost of the regulation may equal or outweigh the projected benefits.

Response: EPA believes that regulating perchlorate in drinking water presents a meaningful opportunity for health risk reduction. EPA believes that regulating perchlorate in drinking water presents a meaningful opportunity for health risk reduction. This determination is based on the best available peer reviewed science and data collected in accordance with accepted methods related to perchlorate's occurrence in drinking water , the presence of perchlorate in foods and the potential health effects of exposure to perchlorate, and EPA's population exposure evaluation as described in more detail in the final regulatory determination. EPA has not performed a cost/benefit analysis for this final determination. EPA will perform such an analysis, as required by SDWA § 1412(3)(C), for the proposed regulation. The Agency has analyzed occurrence data from the Unregulated Contaminant Monitoring Rule (UCMR), which is nationally representative, and found that perchlorate occurred in 26 states and 2 territories affecting millions of people

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Commenter Name: Michael Dourson
Commenter Organization: Toxicology Excellence for Risk Assessment
EPA Document ID: EPA-HQ-OW-2008-0692-1562
EPA Comment ID: 20640
EPA Comment Code: 6110

Comment: Acknowledgements

The authors have collectively studied the toxicity of perchlorate since 1991 on behalf of US EPA and the nonprofit corporation Toxicology Excellence for Risk Assessment (TERA) at the request of the Perchlorate Study Group. Opinions expressed in this commentary, however, reflect solely those of the authors and not of any organization or other individual. Resources to support this technical commentary were provided by the Perchlorate Study Group, based in part on work supported by the developmental reserve fund of TERA.

Summary

We agree with EPA's decision to not regulate perchlorate on a national level at this time. Although the data do provide support for the conclusion that at sufficiently high doses, perchlorate may have adverse effects on sensitive groups within the US population, we agree with EPA's analysis that

perchlorate is not occurring in the public water supply at levels that cause concern for health risks. In particular, EPA's analysis of relative source contribution based on the FDA Total Diet Study and estimates of exposure based on the NHANES/UCR data give an excellent understanding of the potential for exposure for pregnant women, the sensitive population for perchlorate exposure.

Response: Please see the response to comment code 6110. As the federal register notice explains in greater detail, EPA has determined that, pursuant to the NRC's findings, infants and developing children are additional sensitive populations.

Commenter Name: Michael Dourson
Commenter Organization: Toxicology Excellence for Risk Assessment
EPA Document ID: EPA-HQ-OW-2008-0692-1562
EPA Comment ID: 20643
EPA Comment Code: 6110

Comment: Conclusion

In this Federal Register notice, EPA is making a preliminary regulatory determination that a national primary drinking water rule is not necessary for perchlorate because a national primary drinking water regulation would not provide a meaningful opportunity to reduce health risk. In addition, EPA is announcing its plans to publish a Health Advisory, which will provide Federal, Regional, State, and Local public health officials with information regarding health risks posed from perchlorate-contaminated drinking water. Based on EPA's analysis of exposure data and relative source contribution, we agree that perchlorate is not occurring in the public water supply at levels that cause concern for health risks. However, we also recommend that EPA update its RfD prior to publishing a Health Advisory for the following reasons:

* Additional important data on pregnant women and their offspring have become available since the time of the development of the EPA's RfD in 2005, which necessitate a reconsideration of the existing value. This reconsideration is consistent with recommendations of the NAS (2005) in its report.

* The excellent relative source contribution evaluation of EPA, based on well supported and clearly described work of the FDA, necessitates a rethinking of the any RfD, since the underlying studies may not have measured perchlorate in the food of the human subjects.

* The 2005 "RfD" of the NAS does not follow the existing EPA method.

References

Barnes DG, Dourson ML. 1988. Reference dose (RfD): Description and use in health risk assessments. Regul Toxicol Pharmacol 8: 471-486.

Environmental Protection Agency. 2002. A review of the Reference Dose (RfD) and Reference Concentration (RfC) processes. Risk Assessment Forum. EPA/630/P- 02/002F, December.

Environmental Protection Agency. 2008. Integrated Risk Information System (IRIS). Online at www.epa.government/iris.

Faustman EM, Omenn GS. 2001. Risk Assessment. In: Casarett and Doull's Toxicology: The Basic Science of Poisons (Klaassen CD, ed.). 6th Edition. McGraw-Hill, 92.

Lehman, A.J. and O.G. Fitzhugh. 1954. 100-fold margin of safety. Assoc. Food Drug Off. U.S.Q. Bull. 18:51-58.

National Research Council/National Academy of Sciences (NRC/NAS). 2005. Health Implications of Perchlorate Ingestion. NAS Press, Washington D.C.

Strawson J, Zhao Q, Dourson M. 2004. Reference Dose for Perchlorate Based on Thyroid Hormone Change in Pregnant Women as the Critical Effect. Regulatory Toxicology and Pharmacology 39: 44-65.

Tellez RT, Chacon PM, Gibbs J, Crump C, Abarca CR. 2005. Chronic Environmental Exposure To Perchlorate And Thyroid Function During Pregnancy And The Neonatal Period. THYROID: 15(9): 963-975.

Response: Please see the response to comment code 6110. In a NRC 2005 review of the state of the sciences regarding potential perchlorate adverse health effects and mode-of-action ("Health Implications of Perchlorate Ingestion", NRC (2005)), the NRC recommended that data from the Greer et al. (2002) human clinical study be used as the basis for deriving a perchlorate reference dose (RfD) (NRC 2005). From this Greer et al. (2002) human clinical study, the statistical no observed effect level (NOEL) for the perchlorate-induced inhibition of thyroid iodide uptake was determined to be 7.0 ug/kg, which corresponded to an iodide uptake inhibition of 1.8%. NRC concluded that the most health protective and scientifically valid approach to deriving a reference dose for perchlorate, was to base the perchlorate RfD on the inhibition of iodide uptake by the thyroid, and that iodide uptake inhibition, though not an adverse effect per se, is the most appropriate precursor event, and would precede any more severe adverse health effects of perchlorate exposure in humans. The NRC recommended basing the RfD on a precursor to an adverse effect rather than an adverse effect, per se. In this case, NRC used prevention of iodide uptake inhibition, a precursor to adverse thyroid effects, to establish a level at which no adverse effects would be anticipated in exposed populations. This approach is consistent with the Agency's policy on the use of precursor events when appropriate in establishing the critical effect upon which an RfD is based (U.S. EPA, 2002). The NRC recommended that EPA apply an uncertainty factor of 10 to this NOEL of 7.0 ug/kg for the perchlorate-induced inhibition of thyroid iodide uptake, to account for differences in sensitivity between healthy adults and the most sensitive sub-population, consisting of fetuses of pregnant women who might have hypothyroidism or iodide deficiency. EPA has also considered data derived from the Tellez et al. (2005) study. Blood serum perchlorate concentrations predicted through PBPK modeling from data from a study of school children in Chile (Tellez et al. 2005) were within the range of the measured concentrations, and the concentrations of perchlorate in breast milk predicted from the model were within two standard deviations of the measured concentrations. Therefore, PBPK modeling predictions of blood serum perchlorate concentrations were consistent with empirical results, and the predicted extent of iodide inhibition in the most sensitive population (the fetus), based in part on data from Tellez et al. (2005), was not found to be significant at EPA's RfD of 0.7 ug/kg/day.

EPA agrees that additional important data have become available since the RfD was derived in 2005. However, EPA has evaluated the new data and has decided to make the regulatory determination based upon the current RfD. EPA will continue to evaluate any new perchlorate data to determine its relevance to the regulatory determination in accordance with the SDWA.

Greer MA, Goodman G, Pleus RC, Greer SE. Health effects assessment for environmental perchlorate contamination: the dose response for inhibition of thyroidal radioiodine uptake in humans. Environ Health Perspect. 2002 Sep;110(9):927-37. Erratum in: Environ Health Perspect. 2005 Nov;113(11):A732. National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academies Press, Board on Environmental Studies and Toxicology, January, 2005, Washington, D.C. 276pp. Téllez RT, Chacón PM, Abarca CR, Blount BC, Van Landingham CB, Crump KS, Gibbs JP. Long-Term Environmental Exposure to Perchlorate Through Drinking Water and Thyroid Function During Pregnancy and the Neonatal Period. Thyroid. 2005 Sep;15(9): 963-75.USEPA. 2002. A review of the reference dose and reference concentration processes. Risk Assessment Forum, Washington, DC; EPA/630/P–02/0002F.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1748
EPA Comment ID: 20653
EPA Comment Code: 6110

Comment: P.O. Box 13222 Sacramento, CA 95813 November 18, 2008

Dr. Deborah L. Swackhamer, Chair Science Advisory Board Environmental Protection Agency

Dr. Joan Rose Chair SAB Drinking Water Committee Environmental Protection Agency

Dear Dr. Swackhamer and Dr. Rose:

We read with great interest your November 5, 2008 letter to Administrator Johnson concerning EPA's preliminary determination on a national drinking water standard for perchlorate. This letter states that "the SAB strongly believes that there must be a compelling scientific basis to support a determination not to regulate perchlorate..." We completely agree. Through the efforts of EPA's Office of Water, Office of Solid Waste and Emergency Response, and Office of Research and Development over the last decade, the Agency has developed this compelling scientific basis.

First, the overall scientific literature concerning perchlorate's potential effects on human health is extensive. There are very few compounds subject to EPA regulation that can rest on multiple pillars of scientific evidence, including animal studies in multiple species, occupational studies, environmental epidemiology studies, and human clinical trials. There are also very few compounds in which the mechanism of action is clear and occurs with welldefined, non-adverse precursors. And, there are very few compounds that have been subject to a rigorous and comprehensive National Academy of Sciences (NAS) review of the health effects.

As the NAS panel stated, unless these precursor effects occur, the subsequent adverse effects will not occur. To cite the NAS report,

The committee emphasizes that inhibition of iodide uptake by the thyroid has been the only consistently documented effect of perchlorate exposure in humans. The continuum of possible effects of iodide-uptake inhibition caused by perchlorate exposure is only proposed and has not been demonstrated in humans exposed to perchlorate (with the exception that in patients with hyperthyroidism doses of 200 mg daily or higher may reduce thyroid secretion). More important, the outcomes at the end of the continuum are not inevitable consequences of perchlorate exposure.[FN1: National Academy of Sciences, Health Implications of Perchlorate Ingestion, 2005, at 165 (pdf version). The noted dose of 200 mg/d is a conservative therapeutic value. When use of perchlorate to treat hyperthyroidism was common, doses of 400 mg/d were commonly prescribed, but were found to be slow to control thyrotoxicity and doses needed to be repeated 4 to 5 times/d, due to the rapid excretion of the drug. Although it still took an average of 9.4 weeks, doses of up to 2000 mg/d were given to reduce hyperthyroidism to a remission state (Wolff, 1998).]

Although no longer the drug of choice in the clinic for treating thyrotoxicosis, perchorate is still used medically. For example, perchlorate is used to treat amiodarone (an antiarrhythmetic agent) induced thyrotoxicosis.[FN2: 2 J. Wolff, Perchlorate and the Thyroid Gland, Pharmacol Rev. 1998; 50(1):89-105.] In other words, except for its deliberate medical use, exposure to perchlorate has not been shown to have caused reduced thyroid function in humans. In addition to the NAS conclusions, newer studies indicate that exposures to perchlorate at environmentally relevant levels have not been demonstrated to cause any effect on the health of persons.[FN3: See, Benjamin C. Blount, et al., Perchlorate Exposure of the US Population, 2001-2002, J Expos. Sci Envtl Epidem. 2006c; Benjamin C. Blount et al., Urinary Perchlorate and Thyroid Hormone Levels in Adolescent and Adult Men and Women Living in the United States, Envtl Health Perspect., 2006b, 1865-71; Rafael Tellez Tellez et al., Chronic Environmental Exposure to Perchlorate Through Drinking Water and Thyroid Function During Pregnancy and the Neonatal Period, Thyroid, 2005, 963-975; Yona Amitai et al., Gestational Exposure to High Perchlorate Concentrations in Drinking Water and Neonatal Thyroxine Levels, Thyroid, 2007, 843-850; Craig Steinmaus et al., Impact of Smoking and Thiocyanate on Perchlorate and Thyroid Hormone Associationsin the 2001-2002 National Health and Nutrition Examination Survey, Envtl Health Perspect, 2007, 1333-38.] The weight-of-evidence suggests that adverse effects do not occur following chronic exposures to perchlorate at doses much greater than the RfD.[FN4: See, Tellez et al., 2005; Amitai et al., 2007; Lewis E. Braverman et al., The Effect of Perchlorate, Thiocyanate, and Nitrate on Thyroid Function in Workers Exposed to Perchlorate Long-Term, J. Clin. Endocrinol. Metab., 2005, at 700.]

Second, this extensive scientific literature has undergone several major peer reviews. EPA convened peer review panels of its draft risk assessments in 1999 and 2002. The University of Nebraska Medical Center convened a State-of-the- Science Symposium and peer review in 2003. From October 2004 to January 2005, the NRC panel of 15 national experts held several meetings and solicited extensive public comment. While the SAB can contribute to the findings of these panels, EPA already has extensive, independent scientific analysis of perchlorate to underpin its final determination.

Response: Administrator Stephen Johnson replied to the SAB on January 9, 2009. The letter is available in EPA's docket ID No. EPA-HQ-OW-2009-0297 for this notice.

Commenter Name: John C. Vest
Commenter Organization: Public Service Department, Town of Mooresville, NC
EPA Document ID: EPA-HQ-OW-2008-0692-1567

EPA Comment ID: 20667
EPA Comment Code: 6110

Comment: John C. Vest, P.E. Public Services Director PO Box 878 Mooresville, NC 28115 (704) 790-4290

November 7, 2008

Water Docket Environmental Protection Agency 1200 Pennsylvania Avenue, NW Washington, DC

RE: Docket ID No. EPA-HQ-OW-2008-0068 Drinking Water: Preliminary Regulatory Determination on Perchlorate

The Public Services Department of the Town of Mooresville, North Carolina agrees with the Environmental Protection Agency's determination that a national primary drinking water regulation (NPDWR) for perchlorate would not present a meaningful opportunity for health risk reduction for persons served by public water systems.

Our determination is based on several factors including research studies submitted by the EPA, NAS/NRC and FDA as well as articles released by accredited organizations. Authorities concur exposure to perchlorate is not limited to public water sources but is also found in food products. Public water sources found with maximum levels of perchlorate affect a small population of the country and would be better managed at a local level. The results of testing by a third party laboratory in 2002 showed no significant level of perchlorate in the Town of Mooresville's drinking water supply. All test results were below the detection limit of 4u/l.

Should you have any questions, please do not hesitate to contact us.

Sincerely,

John C. Vest, P.E. Public Services Director

Response: EPA believes that regulating perchlorate in drinking water presents a meaningful opportunity for health risk reduction. EPA believes that regulating perchlorate in drinking water presents a meaningful opportunity for health risk reduction. This determination is based on the best available peer reviewed science and data collected in accordance with accepted methods related to perchlorate's occurrence in drinking water , the presence of perchlorate in foods and the potential health effects of exposure to perchlorate, and EPA's population exposure evaluation as described in more detail in the final regulatory determination.
Specifically, The Agency analyzed occurrence data from the Unregulated Contaminant Monitoring Rule (UCMR), which is nationally representative, and found that perchlorate occurred in 26 states and 2 territories affecting millions of people. EPA agrees that perchlorate contamination is widespread in foods; however, EPA does not believe that the widespread presence of perchlorate in food overrides the opportunity for public health risk reduction for persons served by PWSs with perchlorate contamination.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-1851
EPA Comment ID: 20740
EPA Comment Code: 6110

Comment: We are over-regulating ourselves to death! The drinking water is safe enough - there's no need to keep upping the bar. This hits people in the pocket book for no good reason.

Response: Please see the response to comment code 6110.

Commenter Name:
Commenter Organization: Ag Council et al
EPA Document ID: EPA-HQ-OW-2008-0692-1987
EPA Comment ID: 20974
EPA Comment Code: 6110

Comment: November 26, 2008

US Environmental Protection Agency Office of Water Docket (Mailcode 2822T) 1200 Pennsylvania Avenue, NW Washington, DC 20460

RE: Docket ID No. EPA-HQ-OW-2008-0692. Comments on US EPA Preliminary Regulatory Determination on Perchlorate.

The undersigned representatives of the California agricultural industry are pleased to submit the following comments regarding US EPA's preliminary regulatory determination on perchlorate. California agriculture is a diverse and important sector of our economy. It is a $37 billion industry that produces over 350 different crop and livestock commodities and generates an estimated $100 billion in related economic activity. California agriculture accounts for approximately 7.5% of all employment and supports over a million on farm jobs. California agriculture is also the leading exporter of agricultural commodities, sending almost 20% of our agricultural production to foreign markets.

Based upon the available scientific studies as well as the available exposure and occurrence data, the undersigned support EPA's decision not to establish a national primary drinking water regulation for perchlorate. Both the US Food and Drug Administration's (FDA) food sampling data and total dietary survey, along with EPA's calculated relative source contribution reveal that total perchlorate exposure in the US population is well below established levels of human health concern, even for sensitive subpopulations.

Response: Please see response to comment code 6110. The Agency presented an extensive evaluation of dietary exposure to perchlorate in the October 2008 and August 2009 Federal Register notices. EPA has used this dietary exposure data to account for the relative source contribution (RSC) of perchlorate from food and derived potential alternative HRLs for 14 life stages using the RfD and life stage-specific exposure information in the August 9, 2009 Federal Register notice. These levels range from 1 ug/L to 47 ug/L. EPA also evaluated the populations exposed to perchlorate from both food and drinking water in the August 2009 Federal Register notice and the final regulatory determination. EPA recognizes that a drinking water regulation would not eliminate perchlorate exposure in drinking water but believes that the reduction in perchlorate exposure

presents a meaningful opportunity for health risk reduction for persons served by PWSs contaminated by perchlorate.

.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21052
EPA Comment Code: 6110

Comment: November 26, 2008

Docket ID No. EPA-HQ-OW-2008-0692 Water Docket U.S. Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Ave., NW Washington, DC 20460

RE: Comments in Response to the EPA Notice, Drinking Water: Preliminary Regulatory Determination on Perchlorate [EPA-HQ-OW-2008-0068; FRL-8727-6] RIN 2040-ZA02

Dear Sir or Madam:

The Perchlorate Study Group (PSG) is pleased to submit comments in response to the above-captioned EPA regulatory proceeding.

Please note that there are two sets of comments.

1. Perchlorate and Human Health in 2008: The Implications of New Science for the EPA Preliminary Determination. The most important issues for consideration by the Agency relate to the state of the science. The unswerving focus of the PSG has been to analyze and make available the best available scientific information. The scientific comments were prepared by Intertox, a highly-respected firm with extensive experience in the scientific considerations relating to perchlorate.

The Intertox report concludes that the scientific evidence supports the Agency's decision not to establish a national primary drinking water standard for perchlorate, because "there is no meaningful opportunity for health risk reduction."

The most important source of scientific information on the human health issues relating to perchlorate is an extensive report undertaken by the National Academies of Science, released in 2005. The NAS report has been relied upon by the EPA in subsequent regulatory actions.

The Intertox scientific comments bring the scientific information up to date, examining studies published after the NAS report. The Intertox study, like the NAS study, does not recommend a level for EPA's possible adoption. The Intertox report finds that even with highly conservative assumptions, there would be "no significant health risk to the most sensitive individuals" at a level of at or below 15 parts per billion.

Response: Please see the response to comment code 6110.

Commenter Name: Michael Girard

Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21054
EPA Comment Code: 6110

Comment: PERCHLORATE AND HUMAN HEALTH IN 2008: THE IMPLICATIONS OF NEW SCIENCE FOR THE EPA PRELIMINARY DETERMINATION COMMENTS IN RESPONSE TO THE EPA NOTICE DRINKING WATER: PRELIMINARY REGULATORY DETERMINATION ON PERCHLORATE [EPA-HQ-OW-2008-0068; FRL-8727-6] RIN 2040-ZA02

FINAL

Prepared for: PERCHLORATE STUDY GROUP

November 25, 2008

Intertox, Inc. 600 Stewart St. Suite 1101 Seattle, WA 98101

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TABLE OF CONTENTS I. INTRODUCTION.....1 II. KEY SCIENTIFIC STUDIES PUBLISHED SINCE 2005.....6 A. ENVIRONMENTAL STUDIES.....6 B. OCCUPATIONAL OR CLINICAL STUDIES.....12 C. BREAST MILK STUDIES.....13 III. IODINE SUFFICIENCY IN THE UNITED STATES.....18 IV. CONCLUSIONS.....20 IV. REFERENCES.....21

LIST OF APPENDICES

APPENDIX A. REVIEW OF BLOUNT ET AL., 2006

LIST OF FIGURES FIGURE 1. URINARY REANALYSIS RESULTS OF THE NHANES DATA.....10 FIGURE 2. PLOTTING OF DATA REPORTED BY DASGUPTA ET AL., 2008 TO ILLUSTRATE THE ASSOCIATION BETWEEN CONCENTRATIONS OF IODINE AND PERCHLORATE IN URINE AND MILK IN LACTATING WOMEN.....15

I. INTRODUCTION

The Environmental Protection Agency (EPA) has released its preliminary regulatory determination on perchlorate for public comment. The EPA is required by the Safe Drinking Water Act (SDWA) to publish Maximum Contaminant Level Goals (MCLG) and national primary drinking water regulations (NPDWR) IF (emphasis added),

(a) the contaminant may have an adverse effect on the health of persons; (b) the contaminant is known to occur in public water systems with a frequency and at levels of public health concern; and

(c) in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems (73 FR 60264).

Based on these criteria, the EPA has presented their rationale in the determination not to set an NPDWR for perchlorate as it would not present "a meaningful opportunity for health risk reduction for persons served by public water systems." This decision was made based on the derivation of a Health Reference Level (HRL) for perchlorate and was calculated to be 15 ppb based on a relative source contribution (RSC) of 62% (73 FR 60276)..

Even a cursory review of the 50 years of perchlorate research shows that the weight of scientific evidence clearly supports EPA's decision.

The purpose of this document is to review the key scientific studies and how these studies support the EPA's findings in the proposed determination. We present a brief review of the National Research Council of the National Academy of Sciences (NRC) assessment and update key studies that have been added to the scientific literature.

Between 1997 and 2002, at least 13 toxicological studies of perchlorate, all using EPA protocols, were conducted in animals; these include pharmacokinetic studies, subchronic studies, developmental studies, immunotoxicology studies, and a multigenerational reproductive study. All studies were conducted over a range of doses and evaluated independently by EPA. Of the many results obtained from this work, the most sensitive target organ was the thyroid gland and its influence on the body. Studies of potential mutagenic effects were conducted but no such effects were found (U.S. EPA, 2002). During the same time period, there were several clinical exposure studies in humans and a number of epidemiologic and ecological studies, some in occupational settings and some in populations exposed to perchlorate via the community drinking-water supply.

[Text Box: The body of science supports the Agency's decision not to establish a national primary drinking water standard as there is no meaningful opportunity for health risk reduction.]

Response: Please see the response to comment code 6110.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21079
EPA Comment Code: 6110

Comment: IV. CONCLUSIONS

The results of this assessment demonstrate that the RfD continues to be a conservative and health-protective toxicity guideline value. As such, perchlorate concentrations in drinking water at or below the HRL proposed by EPA pose no significant health risk to the most sensitive individuals consuming water on a daily basis over a lifetime. Since the release of the RfD, additional studies have been conducted and continue to add to the scientific weight of evidence supporting the RfD (and HRL) as conservative estimates. The RfD and HRL include uncertainty spanning perhaps an order of magnitude, and estimate a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The

EPA has further determined that perchlorate is not found in public water supplies at a frequency and a level that would cause public health concern. Based on this, the EPA has determined that there is not "a meaningful opportunity for health risk reduction for persons served by public water systems" by determining a NPDWR.

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Response: Please see the response to comment code 6110. EPA estimates that at least 5.1 to 16.6 million people are served by PWSs, for which we have data, that have perchlorate contamination. EPA has determined that an NPDWR for perchlorate could reduce exposures for these populations to levels below the potential alternative HRLs that EPA has identified as levels of public health concern for perchlorate.
EPA believes that this perchlorate exposure reduction presents a meaningful opportunity for the reduction of health risks for persons served by PWSs.

This determination is based on the best available peer reviewed science and data collected in accordance with accepted methods related to perchlorate's occurrence in drinking water, the presence of perchlorate in foods and the potential health effects of exposure to perchlorate, and EPA's population exposure evaluation as described in more detail in the final regulatory determination.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21089
EPA Comment Code: 6110

Comment: US Environmental Protection Agency Office of Water Docket (Mailcode 2822T) 1200 Pennsylvania Avenue, NW Washington, DC 20460

November 10, 2008

Re: Comments in Response to EPA Notice Drinking Water: Preliminary Regulatory Determination on Perchlorate [EPA-HQ-OW-2008-0692; FRL-8727-6].

The Perchlorate Study Group (PSG) is pleased to submit comments to the Environmental Protection Agency (EPA) on Docket ID No. EPA-HQ-OW-2008-0692, entitled Drinking Water: Preliminary Regulatory Determination on Perchlorate. As manufacturers and users of perchlorate, the PSG is committed to ensuring that the best available science is provided in public debate and applied in the subsequent setting of regulatory standards. The member companies of the PSG include Aerojet, American Pacific Corporation (AMPAC), Alliant Techsystems (ATK), and Tronox.

For over ten years, the PSG has worked cooperatively and effectively with the US Environmental Protection Agency (EPA) and other federal agencies, state governments, and water purveyors to:

* increase scientific and medical understanding of perchlorate's possible effects on human health; and,

* assess the level of perchlorate in drinking water that is expected to pose no adverse effects to human health.

We therefore appreciate this opportunity to submit these comments relating to EPA's preliminary determination.

I. The EPA's Proposed Determination is Backed by the Best Science and the Statute

The PSG agrees with EPA's preliminary determination that a Federal drinking water regulation would not meet the SDWA criteria and that EPA has ample justification for this determination. EPA has an extraordinary wealth of comprehensive, authoritative scientific information relating to perchlorate's health effects, supplemented by extensive occurrence and exposure data. The Agency is therefore exceptionally well-positioned to issue a well-considered regulatory determination. The best available scientific data supports a determination under the Safe Drinking Water Act (SDWA) that public water systems do not present a meaningful opportunity for risk reduction.

Response: Please see the response to comment code 6110.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21092
EPA Comment Code: 6110

Comment: Second, EPA has ample scientific and technical data to make a final determination on or before the planned date of December 2008. As noted in the attached scientific summary, perchlorate is one of the most well-studied chemicals with detailed information on the mechanism of action, dose-response, and health effects. This issue also is not new. EPA released its first draft risk assessment on perchlorate in 1998, followed by a second in 2002. The 2005 NAS report was a comprehensive review of the science. The animal and human studies that have been published since the NAS report reduce the uncertainty and reinforce the NAS panel's finding that there will not be any adverse health effects from perchlorate at environmentally-relevant concentrations.

New studies published since the NAS report increase the weight of evidence that the current RfD protects human health including the most sensitive members of our population. In addition, testimony by Congressional members and witnesses alike have discussed the lengthy amount of time that EPA has spent studying the health effects, urging the agency to issue a determination as soon as practicable. We join them in urging EPA to issue the final determination promptly.

Response: Please see the response to comment code 6110.

Commenter Name: Ed Thomas
Commenter Organization: National Rural Water Association (NRWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0521
EPA Comment ID: 28474
EPA Comment Code: 6110

Comment: Please accept the attached comments. Thank-you ED THOMAS

Attachment

September 18, 2009

U.S. Environmental Protection Agency Office of Water Docket (Mailcode 2822T) 1200 Pennsylvania Ave. NW Washington, DC 20460

RE: Drinking Water: Perchlorate Supplemental Request for Comments (Docket Number: EPA-HQ-OW-2009-0297)

To Whom It May Concern:

NRWA commends EPA for their proposed regulatory determination for perchlorate. We believe the Agency has relied on sound science and that a national standard for perchlorate would not result in a meaningful opportunity for health risk reduction.

Response: Please see the response to comment code 6110.

Commenter Name: Mark S. Mayer
Commenter Organization: South Dakota Department of Environment & Natural Resources (DENR)
EPA Document ID: EPA-HQ-OW-2009-0297-0467
EPA Comment ID: 28478
EPA Comment Code: 6110

Comment: September 18, 2009

Comment Clerk Docket EPA-HQ-OW-2009-0297 U.S. Environmental Protection Agency Mail Code: 2822T 1200 Pennsylvania Avenue, NW Washington, DC 20460

To Whom It May Concern:

Thank you for the opportunity to provide comment on the Perchlorate Supplemental Request as published in the August 19, 2009 (Volume 74, Number 159) Federal Register. We have reviewed the request and offer the comments found in the attachment.

We hope EPA will favorably consider our comments. Thank you again.

Sincerely, Mark S. Mayer, P.E. Natural Resources Administrator SD Drinking Water Program

cc: Jim Taft, Executive Director, Association of Safe Drinking Water Administrators Carol Rushin, Acting EPA Region 8 Administrator Jason Glodt, Senior Policy Advisor, Governor's Office James, Stone, Chair South Dakota Section of the American Water Works Association

Attachment

Perchlorate Supplemental Request Comments by South Dakota Department of Environment and Natural Resources (DENR)

General Comments:

- The South Dakota Department of Environment and Natural Resources (DENR) supports EPA's preliminary decision to not regulate Perchlorate, and finds no reason now to alter that decision. Based on the information obtained from the contaminant candidate list and Unregulated

Contaminant Monitoring processes used by EPA to obtain occurrence data on unregulated contaminates, Perchlorate is not a drinking water issue in South Dakota. Consequently, South Dakota does not support EPA establishing a new national regulation for Perchlorate. Such a new rule will become another regulatory burden for our drinking water systems, but it would have no positive health effects or benefits for their customers.

Response: Please see the response to comment code 6110.

Commenter Name: Julie L. Heckman
Commenter Organization: American Pyrotechnics Association (APA)
EPA Document ID: EPA-HQ-OW-2009-0297-0522
EPA Comment ID: 28490
EPA Comment Code: 6110

Comment: The premature or excessive regulation of perchlorate absent full consideration of all the facts and all the science, particularly for so new a concern, would threaten the fireworks industry's ability to continue to serve the country. It would threaten the nation's ability to continue to respect the most patriotic of its traditions.

Response: Please see the response to comment code 6110. Today's determination is based upon an assessment of the best available science and information.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0653
EPA Comment ID: 28556
EPA Comment Code: 6110

Comment: The PBPK modeling is useful in demonstrating that all identified lifestages are protected at the RfD level, and especially under the current HAL of 15 ppb perchlorate in drinking water as they are within the 10x intraspecies factor. The alternative methods of exposure assessment are informative but do not show that any deviation from EPA's typical risk assessment based on a 70 kg adult consuming two liters of water is warranted. As the occurrence of perchlorate in water supplies is sporadic and geographically discreet, the Agency has not provided sufficient information or explanation to justify using Bayesian analyses of water occurrence data. EPA has sufficient information to determine that perchlorate should not be regulated as a drinking water contaminant under the Safe Drinking Water Act and should maintain a recommended health advisory limit of 15 ppb.

Response: Please see the response to comment code 6110. After further consideration of the peer review and public comments, EPA concludes that the PBPK modeling analysis, in the context of the perchlorate regulatory determination, is useful in examining which life stages are most susceptible to the effects of perchlorate. For example, the model indicates that a fetus may be seven times more sensitive to the effects of perchlorate than a pregnant woman. The model also allows for the estimation of the concentration of perchlorate in breast milk (thus breast-fed infant exposure) at various maternal perchlorate exposure levels. However, because of the stated limitations, EPA has decided the model does not directly bear on the current decision regarding the need for a NPDWR

for perchlorate. EPA is continuing to evaluate whether the model could be used in setting a NPDWR for perchlorate.

EPA believes that perchlorate contamination in drinking water does not occur sporadically. The Agency analyzed occurrence data from the Unregulated Contaminant Monitoring Rule (UCMR), which is nationally representative, and found that perchlorate occurred in 26 states and 2 territories.

EPA continues to evaluate the utility of the Bayesian model(s) in the development of a NPDWR for perchlorate.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0653
EPA Comment ID: 28557
EPA Comment Code: 6110

Comment: Attachment

The Environmental Protection Agency (EPA) has sufficient information to make a regulatory determination concerning perchlorate under the Safe Drinking Water Act (SDWA) - perchlorate does not meet the three criteria necessary for regulation - therefore, the Administrator can determine that the EPA should maintain its guidance for a Health Advisory Limit (HAL) at 15 parts per billion (ppb) in drinking water and can decide not to regulate perchlorate under the SDWA. The Agency continues to waste public resources and time based on ill- informed critiques of the National Research Council (NRC) 2005 findings on perchlorate.

Response: Please see response to comment code 6110.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0653
EPA Comment ID: 28562
EPA Comment Code: 6110

Comment: In summary, the PBPK modeling is useful in demonstrating that all identified lifestages are protected at the RfD level, and especially under the current HAL of 15 ppb perchlorate in drinking water as they are within the 10x intraspecies factor in terms of potential risk. The alternative methods of exposure assessment are informative but do not show that any deviation from EPA's typical risk assessment based on a 70 kg adult consuming two liters of water is warranted. As the occurrence of perchlorate in water supplies is sporadic and geographically discreet, the Agency has not provided sufficient information or explanation to justify using Bayesian analyses of water occurrence data. EPA has sufficient information to determine that perchlorate should not be regulated as a drinking water contaminant under the Safe Drinking Water Act and should maintain a recommended health advisory limit of 15 ppb.

Response: Please see response to comment ID 28556 under comment code 6110.

Commenter Name: Sonia Salas

Commenter Organization: Western Growers Association on behalf of several California agriculture groups
EPA Document ID: EPA-HQ-OW-2009-0297-0652
EPA Comment ID: 28683
EPA Comment Code: 6110

Comment: Conclusion

Based upon the best available scientific evidence, including exposure and occurrence data developed since the National Academy of Sciences issued its findings in January, 2005, the undersigned conclude that the regulatory thresholds contemplated in EPA's above referenced notice are not scientifically justified and are substantially more stringent than necessary to ensure protection of public health. Moreover, the US Food and Drug Administration's (FDA) food sampling data and total dietary survey, and the relative source contribution calculated by USEPA for its 2008 preliminary regulatory determination demonstrate conclusively that total perchlorate exposure in the US population is well below established levels of human health concern for both the general public and sensitive subpopulations.

For the reasons articulated above, the California agricultural industry encourages USEPA to act on its October 10, 2008 preliminary regulatory determination for perchlorate, which the weight of scientific evidence demonstrates to be highly health protective. We appreciate USEPA's consideration of our comments and we remain committed to working with USEPA, USDA and FDA to preserve the safety and integrity of our products and their contribution to balanced, healthy diets.

Sincerely, Agricultural Council of California California Citrus Mutual California Cotton Ginners and Growers Association California Farm Bureau Federation California Floral Council California Grape and Tree Fruit League Grower-Shipper Association of Central California Imperial Valley Vegetable Grower Association Ventura County Agricultural Association Nisei Farmers League Ventura County Agricultural Association Western Growers Association Western Plant Health Association Western United Dairymen

Response: Please see the response to comment code 6110.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0647
EPA Comment ID: 28716
EPA Comment Code: 6110

Comment: Introduction

These comments are provided in further support of EPA's preliminary determination that establishment of a perchlorate drinking water standard is not merited, and in reference to comments already posted by Jonathan Borak on September 21st under reference EPA-HQ-OW-2009-0297-0209.1. Mr. Borak's comments refer primarily to the Blount, et al., 2006 study regarding the association of low background levels of perchlorate with thyroid hormone levels. Notwithstanding the many inconsistencies and contradictions in this study as noted by Mr. Borak and others, it is

clear in reviewing other comments submitted under Docket EPA-HQ-OW-2009-0297, that the Blount study is still being heavily relied upon by supporters of perchlorate regulation, who point to this study as proof of the effect of low background levels of perchlorate on thyroid function.

Response: Please see the response to comment code 6110. EPA did consider the data presented in the Blount et al., 2006 study as well as other information on perchlorate exposure. EPA will consider the best available science and information as EPA develops the perchlorate regulation.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0415
EPA Comment ID: 28841
EPA Comment Code: 6110

Comment: Please accept the attached comments on behalf of the American Water Works Association.

Attachment

September 18, 2009

U.S. Environmental Protection Agency Office of Water Docket (Mailcode 2822T) 1200 Pennsylvania Ave. NW Washington, DC 20460

RE: Drinking Water: Perchlorate Supplemental Request for Comments Docket EPA-HQ- OW-2009-0297

The American Water Works Association appreciates the opportunity to comment on the supplemental request for comments regarding perchlorate as detailed in the August 3, 2009 Federal Register notice (74 FR 41883). AWWA is an international, nonprofit, scientific and educational society dedicated to the improvement of drinking water quality and supply. Founded in 1881, the Association is the largest organization of water supply professionals in the world. Our 57,000 members represent the full spectrum of the drinking water community: treatment plant operators and managers, environmental advocates, engineers, scientists, academicians, and others who hold a genuine interest in water supply and public health. Our membership includes more than 4,700 utilities that supply roughly 80 percent of the nation's drinking water. Based on this broad membership base, these comments should be considered as representative of the drinking water community in general.

These comments represent a restatement of the position submitted to the Agency in response to preliminary regulatory determination for perchlorate as detailed in the October 10, 2008 Federal Register notice (73 FR 60262). Given the weight of evidence available at that time and AWWA's independent assessment of occurrence and exposure we concurred with Agency's preliminary determination that regulation of perchlorate would not present "a meaningful opportunity for health risk reduction for persons served by public water systems." We continue to support that preliminary determination. **Response:** Please see the response to comment code 6110.

Commenter Name: Tom Curtis

Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0415
EPA Comment ID: 28857
EPA Comment Code: 6110

Comment: Conclusion

AWWA believes that the Agency's originally proposed decision not to regulate perchlorate is supported by the criteria established in the SDWA. The primary public health issue - as stated by the NRC and others including the Agency's Inspector General [FN22: Wilson, M. 2008. Scientific Analysis of Perchlorate. US Environmental Protection Agency, Office of Inspector General:Washington DC. Available at http://www.epa.gov/oigearth/reports/2009/20081230-2008-0010.pdf] - is iodine deficiency. The SDWA is not an effective means or "tool" to manage a public health issue dominated by dietary issues. The public's exposure to all sources of goitrogens due to extensive contributions from other sources as demonstrated by the FDA food market assessment support the findings that regulation of drinking water would not have a meaningful impact on changing the nation's level of iodine deficiency. A precautionary approach is not justified by the available public health data that provides no indication of epidemic cretinism, goiter, or hypothyroidism, even given the loading of other goitrogens that far exceed potential contribution from perchlorate from all sources. A risk management approach that seeks to extract 100 percent of the risk reduction value from the smallest possible source is not only ineffective, but is a disservice to the mission of seeking the greatest protection of public health. The Agency should use the findings of this assessment to support a collaborative effort with the Department of Health and Human Services and Department of Agriculture to develop outreach materials that communicate the importance of proper dietary levels of iodine, specifically targeting sensitive subpopulations. Attempts have been made in the past to ensure the public received appropriate iodine levels.[FN23: Medicine: Pass the iodized salt, in Time 1949, 19 September. Available at http://www.time.com/time/magazine/article/0,9171,800702,00.html] AWWA believes that remains a better approach for addressing the problem of iodine deficiency, instead of using the Safe Drinking Water Act to address this issue

AWWA appreciates the opportunity to comment on these important drinking water issues. If you have any questions about these comments, please feel to call Kevin Morley or me in our Washington Office at 202-628-8303.

Sincerely, Tom Curtis Deputy Executive Director-Government Affairs

cc: Peter Silva, OW Cynthia Doughtery, OGWDW Eric Burneson, OGWDW

Response: Please see the response to comment code 6110. EPA agrees that promoting iodide nutrition is good public health policy that has a role in reducing the adverse effects associated with exposure to perchlorate. However, the Agency is required to undertake the development of a national primary drinking water regulation if the provisions under section 1412(b)(1) of SDWA are satisfied. That is, if the three legislative criteria are met, EPA must undertake the development of a NPDWR. EPA has determined that the three criteria are met for perchlorate for the reasons outlined in today's federal register notice.

Commenter Name:

Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28875
EPA Comment Code: 6110

Comment: EPA, based on a scientific assessment of the literature in 2008, concluded that federal regulation of perchlorate in drinking water is unwarranted. More than 50 years of scientific research and guidelines support the Agency's position.

I. INTRODUCTION

On August 19, 2009, the Environmental Protection Agency (EPA) issued a Federal Register (FR) notice requesting comments on additional approaches to analyzing data related to EPA's perchlorate regulatory determination (the Notice; U.S. EPA, 2009b). The Notice states that "these additional comments are sought in an effort to ensure consideration of all the potential options for evaluating whether there is a meaningful opportunity for human health risk reduction of perchlorate through a national primary drinking water rule." This document responds to EPA's request for comments on behalf of the Perchlorate Study Group (PSG).[FN1: The PSG member companies include Aerojet General Corporation, American Pacific Corporation, ATK, and Lockheed Martin Corporation.]

EPA is required by the Safe Drinking Water Act (SDWA) to publish Maximum Contaminant Level Goals (MCLGs) and National Primary Drinking Water Regulations (NPDWR) if all the following statutory requirements are met:

(a) the contaminant may have an adverse effect on the health of persons;

(b) the contaminant is known to occur in public water systems with a frequency and at levels of public health concern; and

(c) in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems (U.S. EPA, 1996).

EPA's statutory criteria for setting a standard are unmet in this case. At exposure levels anticipated under the drinking water program, the toxicological literature for perchlorate has demonstrated no adverse effect on human health. Second, data from EPA's first cycle of the Unregulated Contaminant Monitoring Rule (UCMR1) demonstrates that perchlorate does not consistently occur in public water systems at levels that may cause adverse effects in humans. Lastly, because the first two requirements are not met, there is no meaningful opportunity for health risk reduction, the third requirement.

In 2008, EPA concluded that perchlorate did not meet the SDWA requirements and released its preliminary regulatory determination on perchlorate for public comment (U.S. EPA, 2008a). EPA decided not to set an NPDWR for perchlorate as it would not present "a meaningful opportunity for health risk reduction for persons served by public water systems." This decision was based on a Health Reference Level (HRL) for perchlorate in drinking water of 15 ppb, calculated based on an assumed relative source contribution (RSC) for drinking water of 62% of the reference dose (RfD) (U.S. EPA, 2008a).

Data on perchlorate exposure in humans support EPA's preliminary regulatory determination. Any chemical at a sufficient dose will cause an adverse effect. Since the inception of EPA's evaluation of perchlorate and its interim guidance, no evidence of adverse effects from exposure to perchlorate at environmental levels in the U.S. has been presented.[FN2: In 1992, EPA began to address "...concerns about the potential human health effects of perchlorate discovered in drinking water..." and the EPA Superfund Technical Support Center proposed a "provisional" RfD for perchlorate of 0.0001 mg/kg-d which translates to a drinking water equivalent level (DWEL) of 4 ppb (Dollarhide, 1992). In 1995 the provisional RfD was revised by EPA and the National Center for Environmental Assessment (NCEA) to a range that translates from a DWEL of 4 to 18 ppb (Dollarhide, 1995). EPA released a document detailing the derivation of a revised provisional RfD for perchlorate (U.S. EPA, 1998a). In this analysis, EPA focused on potential secondary effects of perchlorate exposure in the developing organism. In 1999, EPA issued was what is referred to as the "1999 Interim Guidance" (Noonan, 1999). EPA states, "...the Office of Research and Development (ORD) recommends that the Agency's risk assessors and risk managers continue to use the standing provisional RfD range of 0.0001 to 0.0005 mg/kg-d [4 to 18 ppb equivalent] for perchlorate-related assessment activities." At the same time, the EPA's Office of Water added perchlorate to the Contaminant Candidate List (CCL) and perchlorate was added to the UCMR (U.S. EPA, 1999). In 2003, EPA's Assistant Administrator issued a Memorandum stating, "...we are re-affirming this guidance with an added suggestion to carefully consider the low end of the provisional 4-18 ppb range."]

50 years of perchlorate toxicological research shows that the scientific weight- of-evidence decidedly supports EPA's preliminary regulatory determination on perchlorate.

A review of the 50 years of perchlorate toxicological research shows that the weight of scientific evidence decidedly supports EPA's preliminary regulatory determination on perchlorate. Furthermore, EPA requested manufacturers and users to fund specific scientific studies on the health effects of perchlorate. As a result, at least 12 animal studies that cover reproductive and developmental toxicity, carcinogenicity, endocrine effects, and other specific toxicological endpoints were funded and conducted.[FN3: For example, the following animal studies were required by EPA to fill data gaps: Argus Research Laboratories, Inc., 1998; Argus Research Laboratories, Inc., 1999; Kiel et al., 1998, 1999; Argus Research Laboratories, Inc., 2001; Primedica, 2001; Bekkedahl et al., 2000; BRT, 2000a, 2000b; Siglin et al., 2000; York et al., 2001a, 2001b.] The results of the studies were transmitted directly to EPA for analysis and without review from industry.

Response: Please see the response to comment code 6110.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28905
EPA Comment Code: 6110

Comment: In summary, EPA's existing, scientifically based RfD remains a conservative, healthprotective toxicity guideline value. Perchlorate concentrations in drinking water at or below the 15 ppb HRL set by EPA, along with its existing, preliminary determination, pose no significant health risk, even to the most sensitive individuals consuming water on a daily basis over a lifetime.

Finally, the best available science establishes that none of the three requirements of the SDWA are met; therefore, there is no scientific justification to regulate perchlorate under this statute.

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APPENDIX A

SUPPLEMENTAL TABLES

Table 1. Comparison of body weights from Kahn and Stralka (2008) and NHANES 1996-2000 in lbs. [see PDF docket ID EPA-HQ-OW-2009-0297-0662]

Table 2. Alternative HRLs based on corrected water intake rates. [see PDF docket ID EPA-HQ-OW-2009-0297-0662]

Table 3. Comparison of daily water ingestion to blood volume. [see PDF docket ID EPA-HQ-OW-2009-0297-0662]

Response: Please see the response to comment code 6110. EPA continues to support the RfD. EPA has determined that perchlorate meets the criteria for regulating a contaminant in Section 1412(b)(1)(A) of SDWA. As previously discussed in this notice, perchlorate may have an adverse effect on the health of persons and perchlorate is known to occur or there is a substantial likelihood that perchlorate will occur in public water systems with a frequency and at levels of public health concern. Moreover, in light of the discussion in this notice and the information available at this time, the Administrator finds that regulation of perchlorate in drinking water systems presents a meaningful opportunity for health risk reduction for persons served by public water systems. Therefore, EPA will initiate the process of proposing a NPDWR for perchlorate.

EPA Comment Code: 6120 Comments urging EPA to regulate perchlorate

Response to Code 6120: EPA has determined that the following three SDWA criteria for regulatory determination have been met for perchlorate: (1) It may have an adverse effect on the health of persons; (2) It is known to occur or there is a substantial likelihood that perchlorate will occur with a frequency and at levels of public health concern in public water systems; and (3) In the sole judgment of the Administrator, regulation of perchlorate presents a meaningful opportunity for health risk reduction for persons served by public water systems. EPA is initiating the development of a proposed NPDWR for perchlorate. EPA intends to publish a proposed regulation and analyses required by SDWA for public review and comment within 24 months of this notice. EPA will consider the public comments and expects to promulgate a final regulation within 18 months of the proposal

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Individual Comments
Commenter Name: B. Halper
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0080
EPA Comment ID: 19675
EPA Comment Code: 6120

Comment: Please regulate the contaminate perchlorate in out drinking water here in AZ to at least the same standards as CA has of 6ppb. The truth of the matter is that the standard should be set as 2 or 3 ppb, but I know this will never happen as long as the DEPT of Defense interferes with this matter and scientific data is tampered with. This current deregulation costs our country millions with medical problems associated with perchlorate and what this does to our children.

Response: See response to comment code 6120.

Commenter Name: Beatrice Williams-Rude
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0083
EPA Comment ID: 19676
EPA Comment Code: 6120

Comment: No downgrading drinking water! No! Not from any source or for any claimed reason.

Beatrice Williams-Rude

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0085
EPA Comment ID: 19677
EPA Comment Code: 6120

Comment: I believe the proposed decision is harmful to public health. Limits on perchlorate should not be increased.

Response: See response to comment code 6120.

Commenter Name:
Commenter Organization: Amherst Family Health Center
EPA Document ID: EPA-HQ-OW-2008-0692-0087
EPA Comment ID: 19678
EPA Comment Code: 6120

Comment: this is bad for my patients health.

Response: This is not a comment, no response needed.

Commenter Name: D.R. Miller
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0089
EPA Comment ID: 19679
EPA Comment Code: 6120

Comment: I strongly oppose perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0090
EPA Comment ID: 19680
EPA Comment Code: 6120

Comment: I would like to see the EPA, an organization which my taxes support, regulate any chemicals deemed harmful to humans in our drinking water.

Thank you.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0091
EPA Comment ID: 19681
EPA Comment Code: 6120

Comment: If you don't protect our drinking water, you don't care about America. Bottom Line.

Response: This is not a comment, no response necessary.

Commenter Name: Nancy Zorn
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0095
EPA Comment ID: 19682
EPA Comment Code: 6120

Comment: I am a private citizen protesting the high amount of perchlorate now allowed n drinking water. I believe this level is unsafe for pregnant women and young children and should not be allowed. I don't belong to any government organization and thought this was a puoblic forum. I am a retired public high school teacher. My name is Nancy Zorn and I live at 7121 N. Comanche Ave., Warr Acres, OK 73132-6629.

Response: See response to comment code 6120.

Commenter Name: Burton Jaffe, MD
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0096
EPA Comment ID: 19683
EPA Comment Code: 6120

Comment: As a physician I am very upset that the EPA does not fully protect me, my family, and all citizens from perchlorate in tap water. You are the environmental protection agency, and I strongly urge you to protect us. Burton Jaffe, MD

Response: See response to comment code 6120.

Commenter Name: S Kornbluth
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0099
EPA Comment ID: 19684
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPA's refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

Please don't wait to regulate Perchlorate. We already know that it has been linked to thyroid problems in pregnant women, newborns and young children. Not regulating this harmful chemical in our drinking water is unacceptable.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0101
EPA Comment ID: 19685
EPA Comment Code: 6120

Comment: We ordinary citizens rely on our government to keep us safe. Please regulate perchlorate in our water.

Response: See response to comment code 6120.

Commenter Name: H Moseson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0103
EPA Comment ID: 19686
EPA Comment Code: 6120

Comment: Get rid of perchlorate in our water! Current levels are not safe for public health.

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #1 - Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-0081
EPA Comment ID: 19687
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPA's refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

Perchlorate is a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children. Not regulating this harmful chemical in our drinking water is unacceptable.

Perchlorate is found in drinking water in 35 states, and according to the EPA's own data, 16 million Americans are at risk of being exposed to this dangerous chemical.

Response: See response to comment code 6120.

Commenter Name: Mass Mailing #1 - Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-0081
EPA Comment ID: 19687
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPA's refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

Perchlorate is a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children. Not regulating this harmful chemical in our drinking water is unacceptable.

Perchlorate is found in drinking water in 35 states, and according to the EPA's own data, 16 million Americans are at risk of being exposed to this dangerous chemical.

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #2 - Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-0100
EPA Comment ID: 19689
EPA Comment Code: 6120

Comment: The Environmental Protection Agency (EPA), supposedly protecting us against harmful chemicals in our air, water and food, has formally refused to set a drinking- water standard for perchlorate, a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children.

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #2 - Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-0100
EPA Comment ID: 19689
EPA Comment Code: 6120

Comment: The Environmental Protection Agency (EPA), supposedly protecting us against harmful chemicals in our air, water and food, has formally refused to set a drinking- water standard for perchlorate, a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children.

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #2 - Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-0100
EPA Comment ID: 19691
EPA Comment Code: 6120

Comment: The Senate Environment and Public Works Committee has endorsed legislation requiring the EPA to set a federal standard for perchlorate and to monitor levels of the chemical in tap water.

Please regulate perchlorate in our drinking water: Your current decision is harmful to public health.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0105
EPA Comment ID: 19692
EPA Comment Code: 6120

Comment: I would like for the EPA to regulate perchlorate to safe levels for all humans including fetuses, babies and children.

Response: See response to comment code 6120.

Commenter Name: Larry Francis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0107
EPA Comment ID: 19693
EPA Comment Code: 6120

Comment: Please take another look at your decision to ignore the chemical perchlorate in our drinking water. It seems to me that the patriotic thing to do is protect Americans from dangerous chemicals in the environment. Plus, it's your job. Please get to work and set a safe standard for perchlorate, certainly not less than the standard set in 2002.

Hopefully, Larry Francis Applegate, Oregon

Response: See response to comment code 6120.

Commenter Name: Ann Watters
Commenter Organization: Polarity Center of Salem
EPA Document ID: EPA-HQ-OW-2008-0692-0108
EPA Comment ID: 19694
EPA Comment Code: 6120

Comment: This level of Rocket fuel is not suitable for human health... Rocket Fuel should be filtered out of the water supply at its source. You are supposed to be protecting the people in this country from health hazards.. Do your job please.

Response: See response to comment code 6120.

Commenter Name: Alison Dalton
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0111
EPA Comment ID: 19695
EPA Comment Code: 6120

Comment: I believe this decision is harmful to public safety. No perchlorate in our drinking water!

Alison Dalton

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0114
EPA Comment ID: 19696
EPA Comment Code: 6120

Comment: Perchlorate is a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children. Not regulating this harmful chemical in our drinking water is unacceptable.

Response: See response to comment code 6120.

Commenter Name: J.H. Gailey
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0115
EPA Comment ID: 19697
EPA Comment Code: 6120

Comment: As a layman with a little background in chemistry the word "perchlorate" scares me, especially since we are advising people to restrict their use of such cleaners as Chlorox for home use. Perchlorate presents an excess of chlorine to rocket fuel as an oxidizer, but we do not need or want that in our drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0118
EPA Comment ID: 19699
EPA Comment Code: 6120

Comment: Please strongly consider the serious health implications of perchlorate and the risks of unregulated perchlorate levels in our drinking water. This issue affects millions of people and should not be taken lightly.

Response: See response to comment code 6120.

Commenter Name: N Wittenberg
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0120
EPA Comment ID: 19700
EPA Comment Code: 6120

Comment: I think this change shows how grossly negligent the EPA has become. Corporations have poisoned the EPA and I am personally sick and tired of sitting back and watching it happen!!!

Response: This is not a comment, no response necessary.

Commenter Name: Lila Williams
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0121
EPA Comment ID: 19701
EPA Comment Code: 6120

Comment: I think this decision to allow perchlorate in water is harmful to public health. Please do not do it.

Thank you!

Lila

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0124
EPA Comment ID: 19702
EPA Comment Code: 6120

Comment: If my generation had enough Perchlorate, I don't think my children and grandchildren should get more than we had. NO MORE PERCHLORATE!

Response: See response to comment code 6120.

Commenter Name: Melissa Mandel
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0125
EPA Comment ID: 19703
EPA Comment Code: 6120

Comment: When I recently moved from California to Phoenix Arizona I learned that the local water supply is contaminated with Perchlorate. The EPA had the responsibility to prevent such contamination at the time it was occurring. Since that did not happen it must protect the public health by controlling the legal limit. Raising the limit does not make any sense given the onslaught of contaminants assaulting the public from all angles. If anything, it should be lowered (since cleanup is not possible).

Please at least do not raise the legal limit.

Melissa Mandel

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0127
EPA Comment ID: 19704
EPA Comment Code: 6120

Comment: Percholate is not a safe chemical. It is known to cause thyroid problems. Drinking water standards for this chemical should be set by the EPA.

Response: See response to comment code 6120.

Commenter Name: B Gagnon
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0128
EPA Comment ID: 19705
EPA Comment Code: 6120

Comment: Perchlorate is a dangerous chemical and harmful to women and children. It should actually be banned as it is now showing up in milk and lettuce across the nation.

Not strictly regulating this harmful chemical in our drinking water is totally unacceptable.

It is clear the the EPA has come under the control of industry. This outrageous decision to allow more and more perchlorate contaminants to be considered acceptable in our water is just too much.

EPA must remember why the taxpayers pay the salaries of those who work there. The American people and the future generations must be protected from these kinds of exposures.

The Safe Water Drinking Act must be honored and EPA must act in good faith on behalf of the public.

You are killing the people.

Response: See response to comment code 6120.

Commenter Name: N Mayers
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0129
EPA Comment ID: 19706
EPA Comment Code: 6120

Comment: EPA needs to regulate and protect our drinking water from perchlorate, a hazard especially to pregnant women.

Response: See response to comment code 6120.

Commenter Name: D Burnham
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0182
EPA Comment ID: 19707
EPA Comment Code: 6120

Comment: I'm against ANY perchlorate in my water. It NEEDS to be filtered out. It should be BELOW the EPA recommendations.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0185
EPA Comment ID: 19708
EPA Comment Code: 6120

Comment: The EPA must set a federal standard for perchlorate and to monitor levels of the chemical in tap water. Refusing to do so is harmful to public health. Thank you.

Response: See response to comment code 6120.

Commenter Name: T.O. Mellem
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0186
EPA Comment ID: 19709
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPA's refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

Perchlorate has been linked to thyroid problems in pregnant women, newborns and young children. Regulation of this chemical in our dringking water is required or it will make the current credit crunch look like child's play. Please set a standard for perchlorate that will prevent a health risk for million of Americans. I urge you to do so in accordance with the Safe Drinking Water Act.

Response: See response to comment code 6120.

Commenter Name: W Fraser
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0187
EPA Comment ID: 19710
EPA Comment Code: 6120

Comment: Please make sure to set the acceptable perchlorate limit based on the health of children.

Response: See response to comment code 6120.

Commenter Name: S McMillan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0188
EPA Comment ID: 19711
EPA Comment Code: 6120

Comment: I am a mother of three who breastfed each of my children. I had my breastmilk tested for perchlorate, and sure enough, it was present. Can you imagine what it is like to be a mother knowing that you are feeding your precious baby rocket fuel? Think about it... My middle son is autisitc. I beat myself up wondering why. What did I do wrong? I tried to be so healthy. Could it be

because I fed him perchlorate? This is so wrong. Please do not allow this public health threat to continue.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0190
EPA Comment ID: 19712
EPA Comment Code: 6120

Comment: PLEASE!!! We have ENOUGH pollutants attacking us from every where, I have a GREAT idea, how about setting the limit to ZERO? Do we really NEED the extra chemicals in our drinking water, Sometimes I need a little pep, but not JET FUEL!!!!

Response: See response to comment code 6120.

Commenter Name: J Garner
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0195
EPA Comment ID: 19713
EPA Comment Code: 6120

Comment: when you lower the standard of anything you go further into killing self. this is not an advisable thing to do. but since no one in government listens to the people i doubt you will lsiten or care one iota to what i a citizen of America thinks.

Response: See response to comment code 6120.

Commenter Name: Sally Swithers
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0196
EPA Comment ID: 19714
EPA Comment Code: 6120

Comment: You're supposed to PROTECT US! How can you not regulate Perchlorate in our water?????????????!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!! Shame on you.

Sally Swithers Sarasota, Florida

Response: See response to comment code 6120.

Commenter Name: W White
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0132
EPA Comment ID: 19715
EPA Comment Code: 6120

Comment: Please keep perchlorate OUT of our drinking water. Thank you.

Response: See response to comment code 6120.

Commenter Name: Jon Olsen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0134
EPA Comment ID: 19716
EPA Comment Code: 6120

Comment: Regarding the allowance of 15 times the previously allowed (safe amount???) quantity of percholate in drinking water sounds to me like a policy of criminal insanity. Both people an our non-human life forms need water as close to pure as we can get. Rocket fuel in our drinking water is an obscenity. Please think: would you want your baby or grandchild being unwittingly fed such stuff?

Jon Olsen, Maine

Response: See response to comment code 6120.

Commenter Name: David Sparling, M.D., F.A.A.P.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0135
EPA Comment ID: 19721
EPA Comment Code: 6120

Comment: In view of the clear evidence that perchlorate ingestion is associated with sjuppression of thyroid function, the increased susceptibility of the fetus, infant and young child to that suppression, the well known effects of bhypothyroidism on brain development and subsequent adult brain function, and the lack of data identifying any threshold level of perchlorate ingestion below which thyroid safety in the fetus, infant and young child can be assured, I make two recommendations:

1) Until such data are available, published in peer-reviewed journals and confirmed by subsequent studies, there should be no increase in the allowable levels of perchlorate in public drinking water supplies, and

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0140
EPA Comment ID: 19723
EPA Comment Code: 6120

Comment: I'am a pulmonary and critical care physician in Florida. I want to express my deep concern about the EPA's decision on addressing perchlorate in water. This chemical is known to be harmful and exposure through water could pose a serious danger to public health.

Response: See response to comment code 6120.

Commenter Name: Dr Roberta Richardson, MD
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0147
EPA Comment ID: 19724
EPA Comment Code: 6120

Comment: This is a comment regarding the EPA's decision not to set a standard for perchlorate in drinking water.

Perchlorate, a component of rocket fuel, has been associated with thyroid disease in pregnant women, young children, and newborns. It has been found in the drinking water of over half the states. I believe it is necessary for the EPA to set a standard for this compound, for public health and safety. I urge you to reconsider your decision.

Dr. Roberta Richardson, MD

Response: See response to comment code 6120.

Commenter Name: Stephen Couche
Commenter Organization: Community for Earth, First Unitarian Church
EPA Document ID: EPA-HQ-OW-2008-0692-0149
EPA Comment ID: 19725
EPA Comment Code: 6120

Comment: Our Church is in Portland, OR, and although I do not know if Perchlorate is a problem anywhere in this state, if it is water systems anywhere it is a problem and health risk. Based on the knowledge we have of what the effects of Perchlorate exposure can have on people we feel that levels should be kept at the lower level and should not be raised - the health of the people of this country is to precious.

Sincerely, Stephen Couche Community for Earth First Unitarian Church Portland, OR

Response: See response to comment code 6120.

Commenter Name: J Mason
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0145
EPA Comment ID: 19726
EPA Comment Code: 6120

Comment: Perchlorate is a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children. Not regulating this harmful chemical in our drinking water is unacceptable.

Perchlorate is found in drinking water in 35 states, and according to the EPA's own data, 16 million Americans are at risk of being exposed to this dangerous chemical.

Response: See response to comment code 6120.

Commenter Name: J Mason
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0145
EPA Comment ID: 19728
EPA Comment Code: 6120

Comment: My mother and myself are sufferring from thryoid disease.She also has a monoclonal gammopathy which doctors say is probably due to environmental exposure: 40+ years of water quality deterioration & contamination. My own city says our exposure to carcinogens in our "treated" water would affect ONLY those with prolonged exposure of 25 years or more- we lived,and drunk this water for 29 years! I am gravely concerned for my children who also have been exposed to these contaminents for nearly 20 years. Meanwhile,our pure,natural wells are being drained,and exploited by companies who profit; while we, meanwhile, are being poisoned! WHO is advocating for us? WHO will STOP this abuse? It is within your power and was mandated BY the PEOPLE,FOR the PEOPLE that your agency SERVE OUR INTERESTS AND HEALTH-PLEASE DO SO! TIME IS OF THE ESSENCE.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0152
EPA Comment ID: 19729
EPA Comment Code: 6120

Comment: Perchlorate standards should not be allowed to risk unsafe levels in human water supplies. the weakened standards do pose real risks. The link to thyroid problems is documented and EPA failures to protect public health are just not acceptable

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0153
EPA Comment ID: 19730
EPA Comment Code: 6120

Comment: This decision is harmful to public health!

Response: See response to comment code 6120.

Commenter Name: G McDonald-Tune
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0155
EPA Comment ID: 19731

EPA Comment Code: 6120

Comment: This chemical is dangerous--public health is at stake--it should be carefully monitored and regulated

Response: See response to comment code 6120.

Commenter Name: William W. Winship
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0157
EPA Comment ID: 19732
EPA Comment Code: 6120

Comment: I believe that the refusal to set a drinking-water standard for perchlorate reflects a wholesale abandonment of responsibility on the part of the Bush Administration EPA...and is blatantly harmful to public health. The Senate Environment and Public Works Committee has endorsed legislation requiring the EPA to set a federal standard for perchlorate and to monitor levels of the chemical in tap water. Please do so!

Respectfully, William W. Winship

Response: See response to comment code 6120.

Commenter Name: A Roth
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0160
EPA Comment ID: 19734
EPA Comment Code: 6120

Comment: I consider the amount of perchlorate in drinking water a danger to public health

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0161
EPA Comment ID: 19735
EPA Comment Code: 6120

Comment: I find it irresponsible to remove the regulation of perchlorate in sources or potential sources of the drinking water of U.S. residents. Can you demonstrate with data that there is no harm to individuals, including children, infants, and pregnant mothers and the fetuses they carry, from drinking water containing perchlorate at the levels that you have announced you intend to allow (about 15 times higher than the level of perchlorate that the EPA permitted in drinking water in 2002)?

Response: See response to comment code 6120.

Commenter Name: Linda Gurley
Commenter Organization: Gurley Painting
EPA Document ID: EPA-HQ-OW-2008-0692-0162
EPA Comment ID: 19736
EPA Comment Code: 6120

Comment: Docket ID No. EPA-HQ-OW- 2008-0068

I was a resident of Falmouth, Massachusetts. We had to pay for bottled water as the ground water was polluted with fuel from the local Navy airbase. The area around the base is a cancer pocket for breast cancer, the cause being directly linked to the ground polution from the jet fuel. Answer the questions of the women (if living) and their families, how dangerous ground water pollution from jet fuel can effect a population.

Response: This is not a comment, no response necessary.

Commenter Name: Wes Sanders
Commenter Organization: Vermont Interfaith Power & Light
EPA Document ID: EPA-HQ-OW-2008-0692-0163
EPA Comment ID: 19737
EPA Comment Code: 6120

Comment: Raising the "safe" level of perchlorate in drinking water is a palpable danger to the public health.

Response: See response to comment code 6120.

Commenter Name: J Porter
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0164
EPA Comment ID: 19738
EPA Comment Code: 6120

Comment: this decision is harmful to public health!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0166
EPA Comment ID: 19739
EPA Comment Code: 6120

Comment: It is past time to make scientific decisions based on science rather than on expediency or political pressure. The people of this country do not want perchlorate in their water - your mission should be to protect us from this, not to make standards easier for industry or the military.

Response: This is not a comment, no response necessary.

Commenter Name: Ann Marie Nehme, M.P.H., M.D.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0168
EPA Comment ID: 19740
EPA Comment Code: 6120

Comment: I think this is harmful to public health. Ann Marie Nehme, M.P.H., M.D.

Response: This is not a comment, no response necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0169
EPA Comment ID: 19741
EPA Comment Code: 6120

Comment: I think that it is unsafe and a bad decision for the gov not to set a drinking water standard for the chemical perchlorate in our tap water. This is outrageous in this day and age, especially with all of the technology available in this country to make sure that our water is safe. To allow chemicals in our water which have known/unknown bad consequences to our health is a travesty and cannot be tolerated. I ask you to reconsider this and make sure our water is free of any chemicals which don't belong. There is a reason for the epa..lets not forget what that is. Thank you. No, thank me..I pay the taxes that pay you to do your job for me and my neighbors...keeping our water safe and chemical free!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0172
EPA Comment ID: 19742
EPA Comment Code: 6120

Comment: Thanks, but if its all the same to you, I don't want any perchlorates in my drinking water. In fact, I believe it's your responsibility to ensure this; so please, do your job.

Response: See response to comment code 6120.

Commenter Name: Cheryl Hall
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0174
EPA Comment ID: 19743
EPA Comment Code: 6120

Comment: The current standards for perchlorate in drinking water (with a maximum that is 15 times higher than what was declared safe in 2002) are unacceptable! This decision does not protect our health.

Cheryl Hall, citizen

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0280
EPA Comment ID: 19744
EPA Comment Code: 6120

Comment: Please keep drinking water safe for my son and our family by not allowing harmful chemicals in excess.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0281
EPA Comment ID: 19745
EPA Comment Code: 6120

Comment: This was a poor decision, and will prove to be harmful to public health. I hope that this is reconsidered.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0282
EPA Comment ID: 19746
EPA Comment Code: 6120

Comment: NO Perchlorate!!!!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0289
EPA Comment ID: 19747
EPA Comment Code: 6120

Comment: This is a public comment on Docket ID EPA-HQ-OW-2008-0692, Drinking Water: Preliminary Regulatory Determination on Perchlorate.

As a physician experienced in environmental epidemiology, I urge you to regulate perchlorate under the Clean Water Act. Perchlorate has been adequately documented as a hazardous chemical with

adverse thyroid effects in pregnant mothers and their offspring. Already an estimated 16 million people are exposed to hazardous levels. You must do your job and regulate exposure to this chemical.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0290
EPA Comment ID: 19748
EPA Comment Code: 6120

Comment: Percholate should be regulated more stringently. It is known to cause thyroid problems and it is unconscionable for the EPA to weaken this regulation. Why do you think there is so much more cancer than there used to be. Start doing your job and protect the American people not the corporations.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0291
EPA Comment ID: 19749
EPA Comment Code: 6120

Comment: Please regulate the perchlorate content of our water supply -- It is already 15 times that which was the supposedly safe limit several years ago. Not regulating it according to the effect on the health of our citizens puts all of us at risk. People are more important than business profits.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0292
EPA Comment ID: 19750
EPA Comment Code: 6120

Comment: Please monitor perchlorate! I believe the job of the Environmental Protection Agency is PROTECTION, which means monitoring and preventing contaminated drinking water. Thank you.

Response: See response to comment code 6120.

Commenter Name: Greg Gerritt
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0295
EPA Comment ID: 19751
EPA Comment Code: 6120

Comment: Increasing the amount of perchlorate in water is not a good idea. Do not do this. greg gerritt

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0296
EPA Comment ID: 19752
EPA Comment Code: 6120

Comment: I believe that allowing more rocket fuel in my drinking water will be harmful to my health and the health of my family.

Perchlorate is a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children.

Response: See response to comment code 6120.

Commenter Name: Douglas, J. Feldman, PE
Commenter Organization: Office of Water Resources, Suffolk County Department of Health Services (SCDHS)
EPA Document ID: EPA-HQ-OW-2008-0692-0297
EPA Comment ID: 19754
EPA Comment Code: 6120

Comment: This department suggests that perchlorate is sufficiently prevalent on Long Island and in other jurisdictions to warrant regulation by establishing a maximum contaminant level. This would greatly assist in enforcing remedial action when necessary, as well as to require and encourage impacted properties to connect to a public water supply system when feasible. Thank you for the opportunity to comment on this subject.

Douglas J. Feldman, P.E. Principal Public Health Engineer Office of Water Resources SCDHS 360 Yaphank Ave. Yaphank, NY 11980 Tel (631) 852-5810 Fax (631) 852-5787

Response: See response to comment code 6120.

Commenter Name: Barbara Seiple
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0300
EPA Comment ID: 19755
EPA Comment Code: 6120

Comment: Please hear us, we the people we need regulation for Perchlorate found in our drinking water. We know it can lead to thyroid problems. what is the hold-up 9n getting this regulated?

Barbara Seiple Philadelphia, PA.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0302
EPA Comment ID: 19756
EPA Comment Code: 6120

Comment: Public drinking water that is safe for human consumption is essential. Given that perchlorate has been noted as a causative agent for thyroid disease, especially in pregnant women and young children, the EPA must set more stringent standards that will foster risk reduction and protect the public health.

Response: See response to comment code 6120.

Commenter Name: B Boxer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0233
EPA Comment ID: 19757
EPA Comment Code: 6120

Comment: Go back to the stricter standard. Absence of adequate regulation in this area can lead to the same type of disaster we are experiencing in the economy. Damage to the health of our people and increased costs for health care in future years are likely to be the cost of lax standards.

Response: See response to comment code 6120.

Commenter Name: Craig Leman, M.D.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0234
EPA Comment ID: 19758
EPA Comment Code: 6120

Comment: Perchlorate is a harmful contaminant, and it is definitely in the national interest to find ways to detect and to limit its presence in the environment. Craig Leman. M. D.

Response: See response to comment code 6120.

Commenter Name: Trudi Ferguson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0235
EPA Comment ID: 19759
EPA Comment Code: 6120

Comment: My thoughts on the need to regulate perchlorate in our drinking water is this. Never before in my life have I met more people with Thyroid problems. Including people in my own family. Perchlorate was once used by the medical practices to regulate a person's thyroid. Then it must be very important to keep this away healthy bodies. Children are the most vulnerable and we

don't need to add more chemicals into their systems. If we can prevent it, we should. An ounce of prevention is worth a pound of cure!

Sincerely, Trudi Ferguson

Response: See response to comment code 6120.

Commenter Name: Judith Gardiner
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0238
EPA Comment ID: 19760
EPA Comment Code: 6120

Comment: Protect the general public before industry interests. Please do not allow perchlorate in drinking water at concentrations so much higher than previously thought safe.

Judith K. Gardiner

Response: See response to comment code 6120.

Commenter Name: R. DeLauro
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0239
EPA Comment ID: 19761
EPA Comment Code: 6120

Comment: Allowing Perchlorate in drinking water isn't acceptable. So many people have compromised immune systems, and aren't yet aware of it. Allowing toxins in the water could be considered tantamount to slow, premeditated murder in auto immune cases. How can you allow this?

No amount of poisons are safe in the body. None.

EPA, Environmental PROTECTION Agency. Are you protecting the public or the corporations?

Response: See response to comment code 6120.

Commenter Name: D.E. Wedge
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0244
EPA Comment ID: 19762
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPA's refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

Perchlorate is a highly reactive oxidation agent and has been shown to have significant biological activity damaging to both animals and humans.

I understand it has been detected in large numbers of drinking water sources in the United States, potentially affecting millions of Americans.

The Safe Drinking Water Act mandates that the EPA must set a standard for such substances, in order to protect the health of our citizens.

Thank you, D. E. Wedge 6591 Maplegrove St. Oak Park, CA 91377

Response: See response to comment code 6120.

Commenter Name: C. Curtin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0245
EPA Comment ID: 19763
EPA Comment Code: 6120

Comment: I believe like MDs for social respnsibility that this would be injurious to health.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0248
EPA Comment ID: 19764
EPA Comment Code: 6120

Comment: This decision is harmful topublic health!

Response: See response to comment code 6120.

Commenter Name: T. Davis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0249
EPA Comment ID: 19765
EPA Comment Code: 6120

Comment: Your decision not to set a percholorate standard is harmful to the health of the citizens of the USA. By failing to set a standard, you have not lived up to your mission to product Americans from pollutants. This is shameful.

Response: See response to comment code 6120.

Commenter Name: M. Mandel
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0250
EPA Comment ID: 19766
EPA Comment Code: 6120

Comment: Docket ID No. EPA-HQ-OW- 2008-0068 Drinking Water: Preliminary Regulatory Determination on Perchlorate I recently moved to Phoenix Arizona and learned upon arrival that Perchlorate is a risk factor in the local water supply due to contamination of the ground water. Since the EPA did not protect this vital resource for our health and safety at the time the damage was done, it should at least protect us now and into the future. Raising the legal limit protects the interests of polluters, not the public health. Please do not approve such a change in the regulation of this contaminant. M. Mandel

Response: See response to comment code 6120.

Commenter Name: J.B. Goss
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0251
EPA Comment ID: 19767
EPA Comment Code: 6120

Comment: Against ANY increase in perchlorate. How can you even consider such a thing?

JB Goss

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0254
EPA Comment ID: 19768
EPA Comment Code: 6120

Comment: This seems outrageous to me. We know perchlorate at current levels is harmful to human health -- why on earth do you refuse to regulate it? Thyroid disorders are serious and can compromise the health of this and future generations. Please take better action.

Response: See response to comment code 6120.

Commenter Name: P. Medeiros
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0256
EPA Comment ID: 19769
EPA Comment Code: 6120

Comment: Return regulations to safe levels of perchlorate in water supply and throughout the food chain.

I have high levels I am now experiencing thyroid problems, I face removal of part of my thyroid as the only means to mitigate the signs and symptoms of my thyroid condition.

I see a direct correlation to excess ive levels of perchlorate being allowing into our water supply and food chain.

It is your vested responsibility to oversee environmental conditions to prevent the American people from diseases and conditions detrimental to their health and well being and this issue must be seriously addressed in good faith or you are failing in your responsibilities to citizens. Thank you

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0257
EPA Comment ID: 19770
EPA Comment Code: 6120

Comment: Please regulate perchlorate in drinkng water. Your decision to not regulate perchlorate is harmful to public health. It is 15 times higher than in 2002 and millions of Americans are exposed to unsafe levels. Please do not put people's health at risk.

Response: See response to comment code 6120.

Commenter Name: D. Sawyer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0258
EPA Comment ID: 19771
EPA Comment Code: 6120

Comment: This is harmful to public health !!!!!

Response: This is not a comment, no response is necessary.

Commenter Name: D. Sawyer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0259
EPA Comment ID: 19772
EPA Comment Code: 6120

Comment: This decision is harmful to public health !

Response: This is not a comment, no response is necessary.

Commenter Name: Noel Smith
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0260
EPA Comment ID: 19773
EPA Comment Code: 6120

Comment: Get Serious. The EPA is supposed to protect the health of the environment and US citizens, not aid business. I find this proposal to be appalling. Is there no shame in this administration? Noel Smith, Auburn, Maine

Response: This is not a comment, no response is necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0261
EPA Comment ID: 19774
EPA Comment Code: 6120

Comment: Please regulate our water!

Response: See response to comment code 6120.

Commenter Name: Rick Sandlin
Commenter Organization: Global Wellness and Nutrition
EPA Document ID: EPA-HQ-OW-2008-0692-0264
EPA Comment ID: 19775
EPA Comment Code: 6120

Comment: We are VERY CONCERNED ABOUT THE QUALITY OF OUR TAP WATER TODAY! EPA: Please, No Perchlorate in Our Tap Water! This decision is harmful to public health!

Response: See response to comment code 6120.

Commenter Name:
Commenter Organization: Alliance for Democracy
EPA Document ID: EPA-HQ-OW-2008-0692-0265
EPA Comment ID: 19776
EPA Comment Code: 6120

Comment: I keep hearing that tap water is safer than bottled. Then I get a notice that the EPA does not regulate perchlorate in the Nation's drinking water. In my opinion, it is your major job to see that what people in the United States are eating or drinking are not negatively affected by substances being put into the environment by anyone - persons or corporations.

Response: This is not a comment, a response is not necessary.

Commenter Name: Renee Watkins
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0266
EPA Comment ID: 19777
EPA Comment Code: 6120

Comment: It's wrong to create major health problems for innocent people in order to protect the waste disposal practices of certain entities, public or private, who wish to avoid regulation. You may

think you are protecting economic welfare, but you are actually contributing to the decline of this country, in health and in safety. Renee Watkins

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0268
EPA Comment ID: 19778
EPA Comment Code: 6120

Comment: I feel this decision is harmful to public health!

Response: See response to comment code 6120.

Commenter Name: B. Cramer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0269
EPA Comment ID: 19779
EPA Comment Code: 6120

Comment: The EPA should reverse its decision and set a more stringent standard regulating the amount of perchlorate in drinking water. This dangerous chemical is linked to thyroid problems in pregnant women, newborns and young children. Perchlorate has been found in the drinking water in 35 states in the U.S.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0272
EPA Comment ID: 19780
EPA Comment Code: 6120

Comment: I disagree with the relaxation of perchlorate level standards in our drinking water supplies.

Response: See response to comment code 6120.

Commenter Name: Gerson T Lesser, MD
Commenter Organization: Department of Geriatrics, Mt Sinai School of Medicine
EPA Document ID: EPA-HQ-OW-2008-0692-0277
EPA Comment ID: 19783
EPA Comment Code: 6120

Comment: Gentlemen,

Perchlorate in the water supply is a potential hazard, especially for thyroid disease, and especially in the very young and pregnancy. It would be unwise to loosen restrictions on content of this in drinking water.

G.T. Lesser, MD, Asst Professer

P.S. These comments are mine and not necessarily those of the Medical School.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0206
EPA Comment ID: 19784
EPA Comment Code: 6120

Comment: No perchlorate in my water!!!

Response: See response to comment code 6120.

Commenter Name: J Monson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0209
EPA Comment ID: 19785
EPA Comment Code: 6120

Comment: We need to tighten drinking water restrictions, not loosen them. The general public is already exposed to far too many toxins in America's water supply, from perchlorate to prescription drugs. Loosening the regulations is a bad idea. Please don't change the perchlorate level that is acceptable in our water.

Response: See response to comment code 6120.

Commenter Name: Lisa Bromfield
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0211
EPA Comment ID: 19786
EPA Comment Code: 6120

Comment: Science gives us more and more examples of how the chemicals we are adding to the water and soil of our planet are being found in human bodies. We need LESS chemicals in the water - not more!! Please consider the health of not only humans but the plants and animals with whom we share the planet and on whom we depend.

Sincerely, Lisa Bromfield Stephens City, VA

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0212
EPA Comment ID: 19787
EPA Comment Code: 6120

Comment: No perchlorate in my drinking water!

Response: See response to comment code 6120.

Commenter Name: Alexander N. Gunn II, M.D., FACS
Commenter Organization: Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-0213
EPA Comment ID: 19788
EPA Comment Code: 6120

Comment: I am deeply offended that you would consider allowing near-toxic levels of perchlprate in drinking water. This is a marked derogation of responsibility which is intolerable to the average American citizen. We demand that you reduce this ruling at once.

Sincerely, Alexander N. Gunn II, MD, FACS

Response: See response to comment code 6120.

Commenter Name: Don Thompson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0214
EPA Comment ID: 19789
EPA Comment Code: 6120

Comment: I cannot believe that the proposed level of Perchlorate to be allowed in drinking water is safe. Our town was has just finished a very expensive water treatment facility to reduce the arsenic levels in our drinking water. It was an expenditure which I felt was justified and I believe that the expenditures necessary to lower potentially harmful levels of Perchlorate should also be required.

Sincerely, Don Thompson

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0215
EPA Comment ID: 19790
EPA Comment Code: 6120

Comment: Perchlorate levels in drinking water supplies should be reduced not increased. Perchlorate levels in water are currently unacceptable and should most definitely not have standards that would increase allowable levels.

Response: See response to comment code 6120.

Commenter Name: S.T. Joyce
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0216
EPA Comment ID: 19791
EPA Comment Code: 6120

Comment: This standard is inadequate and unacceptable. When did the EPA become an organization that is not dedicated to protecting citizens?

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0218
EPA Comment ID: 19792
EPA Comment Code: 6120

Comment: I am an individual, living in Palo Alto, CA Perchlorate is KNOWN to be unhealthy. Therefore I consider it IMPERATIVE that regulations be made to limit it. Actually, if we were to use the Precautionary Principle, we would not allow ANY AMOUNT in our water, until it could be proven that some amount was NOT unhealthy/damaging. However since we don't operate that way, and since without regulations, those who produce/ use perchlorate won't bother to be careful, we need a specified limit.

Response: See response to comment code 6120.

Commenter Name: Diana Smith
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0219
EPA Comment ID: 19793
EPA Comment Code: 6120

Comment: EPA-HQ-OW-2008-0692

I think it is important to keep Perchlorate levels very low - at least to 2002 levels thank you.

Diana Smith

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0220
EPA Comment ID: 19794
EPA Comment Code: 6120

Comment: We need to keep our water as pure as possible. There should be NO perchlorate in tap water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0222
EPA Comment ID: 19795
EPA Comment Code: 6120

Comment: A public comment concerning levels of Perchlorate in drinking water. Refusing to regulate this harmful chemical in our drinking water is unacceptable. I urge you to consider the health of the American public, most especially those of highest risk, pregnant women, children and newborns.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0224
EPA Comment ID: 19796
EPA Comment Code: 6120

Comment: Please do not allow perchlorate to contaminate our drinking water. It is a safety hazard that is not necessary and harmful especially to children and pregnant women. Aren't we causing enough harm to our planet and our health without adding a new harmful elememnt that we will need to clean up?

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0226
EPA Comment ID: 19797
EPA Comment Code: 6120

Comment: Please regulate perchulate in drinking water. Our health depends on it. We are exposed to UNSAFE levels of it in OUR drinking water.

Response: See response to comment code 6120.

Commenter Name: Glenn Shean, Ph.D.
Commenter Organization: Hamptom Roads Counseling
EPA Document ID: EPA-HQ-OW-2008-0692-0307
EPA Comment ID: 19798
EPA Comment Code: 6120

Comment: Allowing increased levels of perchorate in our drinking water is a crime. who does the EPA work for industry or the citizens? For the recent past the rhetorical question must be answered as INDUSTRY!

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0308
EPA Comment ID: 19799
EPA Comment Code: 6120

Comment: Perchlorate does not belong in our drinking water - period!

Response: See response to comment code 6120.

Commenter Name: Bonnie Mandell-Rice
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0310
EPA Comment ID: 19800
EPA Comment Code: 6120

Comment: Please do not allow perchlorate in our drinking water. There already are too many chemicals and pharmaceuticals in the water supply. Even if in isolation one such thing would be "safe," we have no idea about how they all interact. We already know perchlorate is dangerous. Do not allow it to be added to the mix.

Bonnie Mandell-Rice Broomfield,CO

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0311
EPA Comment ID: 19801
EPA Comment Code: 6120

Comment: No rocket fuel in my drinking water, please!

You morons shouldn't have to be TOLD something like this!

Nov. 4 couldn't come soon enough!!!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-0313
EPA Comment ID: 19802
EPA Comment Code: 6120

Comment: There should be no perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0314
EPA Comment ID: 19803
EPA Comment Code: 6120

Comment: Unless you're also going to approve insertion of rocket engines into the large intestine, any level of Perchlorate in the water supply in unacceptable.

http://www.youtube.com/watch?v=1rAsoLm1Ges

Thanks for listening.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0317
EPA Comment ID: 19804
EPA Comment Code: 6120

Comment: Perchlorate levels need to be monitored as they can be harmful to the health of many Americans.

Response: See response to comment code 6120.

Commenter Name: Dr. Thomas Clark
Commenter Organization: Southern Appalachian Forestry Task Force (SAFTF)
EPA Document ID: EPA-HQ-OW-2008-0692-0318
EPA Comment ID: 19805
EPA Comment Code: 6120

Comment: The U.S. desperately needs clean water for the health of our children. Please help strengthen the regulations which affect our water supplies.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0319

EPA Comment ID: 19806
EPA Comment Code: 6120

Comment: Why are we putting ourselves at risk when we don't have to??? As a thyroid cancer survivor, I want to know that this chemical, which has been proven to affect the thyroid, is regulated at a safe level. It has been found in the drinking water of 35 states, so we need to do something. Right now we're behind where we were before, not ahead!!! The maximum safe level for perchlorate in drinking water is now 15 times higher than what the EPA declared safe in 2002. According to Physicians for Social Responsibility, under this new standard, more than 16 million Americans are exposed to unsafe levels of perchlorate in their drinking water, and independent analysis shows anywhere from 20 to 40 million Americans at risk. It's time to start making us safer!

Response: See response to comment code 6120.

Commenter Name: Erik Lokensgard
Commenter Organization: Division of the Biological Sciences, University of Chicago
EPA Document ID: EPA-HQ-OW-2008-0692-0320
EPA Comment ID: 19807
EPA Comment Code: 6120

Comment: Concerning: EPA-HQ-OW-2008-0692 Docket Title Drinking Water: Preliminary Regulatory Determination on Perchlorate Docket Type Nonrulemaking Document ID EPA-HQ-OW-2008-0692-0001

October 15, 2008

Dear Reader,

I am a fourth year biology major at the University of Chicago and am deeply concerned about the current dangerously high perchlorate allowance. I recommend that regulations be made immediately limiting the industrial output of perchlorate and perchlorate related compounds. Perchlorate interferes with iodide uptake in the thyroid, and the news of significant levels being found in breast milk and elsewhere is disturbing. If a woman cannot safely breastfeed her child, we are in dire straights indeed.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0321
EPA Comment ID: 19809
EPA Comment Code: 6120

Comment: Are you guys nuts! We don't want 15 times more Perchlorate that we had in 2002. A jet fuel! Shame on you! Do all you people drink bottled water and just think that what people don't know won't hurt them? I drink tap water because I thought I could trust the federal government! Please clean up our water.

Response: See response to comment code 6120.

Commenter Name: Jennifer Sass, PhD
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2008-0692-0322
EPA Comment ID: 19811
EPA Comment Code: 6120

Comment:

October 17, 2008

Docket identification (ID): EPA-HQ-OW-2008-00692

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0323
EPA Comment ID: 19814
EPA Comment Code: 6120

Comment: EPA-HQ-OW- 2008-0068

Why would anyone want to drink anything that's in rocket fuel???

Would you?

Response: This is not a comment, a response is not necessary.

Commenter Name: Sarah Woodwide Gallagher
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0324
EPA Comment ID: 19815
EPA Comment Code: 6120

Comment: Ladies/Gentlemen:

How in good conscience can you countenance endangering the health of Americans with this flawed regulation?

Most sincerely,

Sarah Woodwide Gallagher

Response: This is not a comment, a response is not necessary.

Commenter Name: Clif Steinberg

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0326
EPA Comment ID: 19816
EPA Comment Code: 6120

Comment: It is time to stop the madness. Perchlorate is among the many toxic contaminants that we have poisoned our environment with, and now rather than protect ourselves and clean up our mess we will just drink our own poison. Insanity! Maybe criminal.

-Clif Steinberg

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0331
EPA Comment ID: 19817
EPA Comment Code: 6120

Comment: I want my water regulated and I think that this decision is harmful to our health and needs to be changed.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0333
EPA Comment ID: 19819
EPA Comment Code: 6120

Comment: No... I don't need any more Perchlorate in my water or my atmosphere. I live next to 3M.

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0335
EPA Comment ID: 19820
EPA Comment Code: 6120

Comment: I think this decision is harmful to public health!

Response: See response to comment code 6120.

Commenter Name: Stephen F. Lynch
Commenter Organization: Granite Medical Group
EPA Document ID: EPA-HQ-OW-2008-0692-0336

EPA Comment ID: 19824
EPA Comment Code: 6120

Comment: I am a practicing physician of Internal Medicine and Pediatrics. I have researched the issue of acceptable perchlorate levels in drinking water, and have concluded that the current levels are TOO HIGH, not too low. Allowing higher levels will adversely affect the health of US citizens, including yours! Do NOT raise the current levels.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0337
EPA Comment ID: 19825
EPA Comment Code: 6120

Comment: This is a public comment regarding perchlorate levels in drinking water. I urge you to set reasonable levels for acceptable perchlorate concentrations in drinking water. These levels should be at or below those deemed "safe" by the EPA itself in 2002. The American public has the right to safe drinking water.

Response: See response to comment code 6120.

Commenter Name: D Timmerman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0340
EPA Comment ID: 19826
EPA Comment Code: 6120

Comment: We ask that perchlorate not be added to water. It is a chemical that is very toxic and could lead to ailments to the population.

Response: Perchlorate is not added to water. EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Edith A. Martin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0341
EPA Comment ID: 19828
EPA Comment Code: 6120

Comment: I am an educated consumer and an American citizen. I am against the current allowable level of perchlorate in our drinking water. This is just one more ruling that the EPA has not enforced properly to ensure that the public is protected from known toxins in our environment, whether it is in our air or water. Please ensure the safety of our water in this case by adjusting the level of perchlorate.

Thank you, Edith A. Martin

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0343
EPA Comment ID: 19829
EPA Comment Code: 6120

Comment: Do not allow unsafe chemicals in our water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0344
EPA Comment ID: 19830
EPA Comment Code: 6120

Comment: You're not helping! Perchlorate levels in drinking water as approved by the Bush EPA is unacceptable!

Response: See response to comment code 6120.

Commenter Name: Thomas Armstrong
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0348
EPA Comment ID: 19831
EPA Comment Code: 6120

Comment: Dear EPA,

I do not want perchlorate in my drinking water.

Thomas Armstrong

Response: See response to comment code 6120.

Commenter Name: Lynn and Harrison Houston
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0349
EPA Comment ID: 19832
EPA Comment Code: 6120

Comment: Dear Sirs,

We need a drinking water standard. this is harmful to public health as these chemicals are toxic.

Sincerely, Lynn and Harrison Houston Satellite Beach, Florida 32937-3000

Response: See response to comment code 6120.

Commenter Name: C. Fletcher
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0351
EPA Comment ID: 19833
EPA Comment Code: 6120

Comment: As a registered nurse, I am concerned that no standard regarding the currently allowable amounts of perchlorate in drinking water exists. Perchlorate affects the function of the thyroid gland, a gland that is essential to human health. Perchlorate is found in the water drunk by humans in at least 35 states. It is essential that the EPA set standards for levels of perchlorate in drinking water in order to address the problem and promote public health.

Response: See response to comment code 6120.

Commenter Name: S. McCarthy
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0355
EPA Comment ID: 19836
EPA Comment Code: 6120

Comment: This is an unsafe decision! Perchlorate in drinking water must be limited or E- liminated. Reconsider this decision with its increased danger for our tap water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0359
EPA Comment ID: 19837
EPA Comment Code: 6120

Comment: As a concerned citizen, I urge you to set a cautious standard for regulating perchlorate in drinking water.

I worked at Rocketdyne in Canoga Park in the late 1960's, where I began having thyroid problems for the first time and have subsequently developed autoimmune issues and chemical sensitivities. Please consider that the human immune system can tolerate only a finite amount of toxicity from all sources before it begins to break down. Perchlorate may be only one of many hazards in our water system but that does not make it insignificant enough to overlook.

The role of the Environmental Protection Agency is to protect us from harmful substances. Please exercise diligence in carrying out your role.

Response: See response to comment code 6120.

Commenter Name: Elizabeth Sheehan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0362
EPA Comment ID: 19838
EPA Comment Code: 6120

Comment: I am extremely concerned about the increased risk of exposure to harmful toxins such as perchlorate in tap water. This is a significant public health issue, putting young children, pregnant women, unborn children at risk. I urge you to re-examine your standards of acceptance regarding perchlorate. I thank you for considering my comment and rethinking policies.

Sincerely, Elizabeth Sheehan

Response: See response to comment code 6120.

Commenter Name: M.E. Harte
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0363
EPA Comment ID: 19839
EPA Comment Code: 6120

Comment: please regulate perchlorate in drinking water! That is a known carcinogen and should be regulated. Would you like one of your kids drinking water contaminated with that stuff? Please regulate it. Thanks!

Response: See response to comment code 6120.

Commenter Name: Terrence L. Horan, D.D.S.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0365
EPA Comment ID: 19840
EPA Comment Code: 6120

Comment: EPA representatives, Perchlorate has been show to be detrimental to human health. That is reason enough to restrict its presence in drinking water. Whatever industry has to do to keep it out of our environment, they must be forced to do. Anything less is irresponsible.

Terrence L. Horan, D.D.S.

Response: See response to comment code 6120.

Commenter Name: Robert N. Milling
Commenter Organization: Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-0366
EPA Comment ID: 19841
EPA Comment Code: 6120

Comment: Regulate Pechlorate in drinking water

Response: See response to comment code 6120.

Commenter Name: H.N Hanna
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0367
EPA Comment ID: 19842
EPA Comment Code: 6120

Comment: I am dismayed that the EPA has refused to set an appropriate drinking water standard for perchlorate. This rocket fuel chemical has been linked to thyroid problems in pregnant women, newborns and young children. The maximum safe level is now 15 times higher than what the EPA declared safe in 2002. The new standard puts 20 to 40 million of us at risk. I think the EPA should be doing a better job of protecting us; that is what it was set up to do, and that is what we taxpayers are paying for the EPA to do.

Response: See response to comment code 6120.

Commenter Name: Mary Beth Sullivan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0370
EPA Comment ID: 19843
EPA Comment Code: 6120

Comment: To Whom This May Concern:

I write to insist that the EPA do the job it was created to do, and REGULATE the lowest amount possible of perchlorate in water.

Response: See response to comment code 6120.

Commenter Name: Mary Beth Sullivan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0370
EPA Comment ID: 19845
EPA Comment Code: 6120

Comment: The EPA exists to PROTECT Americans from the predators that manipulate science; PROTECT our children from the chemicals that do them harm (indeed permanent damage). Career scientists at the EPA know the right thing to do on this issue. I beg you to have the courage to do the right thing. Leave politicians and well-funded lobbyists out of this decision.

Please, provide tight regulation on perchlorate.

While you're at it, demand that the polluters pay to clean up the mess they've made -- we all know they've taken an obscene amount of our tax dollars as profit!

Sincerely, Mary Beth Sullivan 212 Centre Street Bath, Maine 04530 207 443 9502 mbsull@mindspring.com

Response: See response to comment code 6120. Requiring polluter payment is outside the scope of this rule; no response is necessary.

Commenter Name: K. Hannigan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0371
EPA Comment ID: 19846
EPA Comment Code: 6120

Comment: Please do not put Perchlorate in our water.

Response: Perchlorate is not added to water.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0372
EPA Comment ID: 19847
EPA Comment Code: 6120

Comment: So it's safe to drink rocket fuel? Really? And we're supposed to believe there are no politics in government science and that the EPA cares about the health of Americans? Really???

Perchlorate is unsafe. If you doubt that, please feel free to administer it to members of your own families but DON'T force citizens counting on clean water to drink it.

Don't become the Environmental Pollution Agency.

Response: This is not a comment, a response is not necessary.

Commenter Name: Judith Weiss
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0374
EPA Comment ID: 19848
EPA Comment Code: 6120

Comment: I understand that the EPA is considering raising the bar on "safe" levels of byproducts of rocket fuel in our drinking water. This is the kind of politically driven lack of concern for citizen health that we've come to expect from our government.

I object to this agency playing cancer roulette with my health and the health of the nation.

Until and unless each water contaminant is tested for safety by the Ames test or another reputable test you should NOT deem any levels of rocket fuel or its byproducts as safe in food water or drink.

Let's see some concern for the public good in your policies. Judith Weiss

Response: See response to comment code 6120.

Commenter Name: Sherrie Riggio
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0375
EPA Comment ID: 19849
EPA Comment Code: 6120

Comment: Please keep the levels of perchlorate in the drinking water at the levels suggested by safety standards declared by the EPA in 2002. It seems like we are going backwards with safety issues instead of forward. The public's health must take priority over politics. Please. Sherrie Riggio.

Response: See response to comment code 6120.

Commenter Name: Peter Roloff
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0376
EPA Comment ID: 19850
EPA Comment Code: 6120

Comment: As a concerned citizen I can think of no permissible levels of Perchlorate that should be allowed in our fresh water sources, period, end of discussion. sincerly, Peter Roloff

Response: See response to comment code 6120.

Commenter Name: J. Koss, MD
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0377
EPA Comment ID: 19851
EPA Comment Code: 6120

Comment: PERCHLORATE, LIKE ALL MAN MADE CHEMICALS POSE UNCERTAIN AND UNTESTED RISKS TO MY PATIENTS. EUROPE demands proof of safety to add chemicals to the environment, let alone drinking water.Adults, especially children, run risks potentially discoverable AFTER 10-20 years of exposure. WHAT WILL THE GOVERNMENT DO THEN? It will be too late for many victims by then.

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0379
EPA Comment ID: 19852
EPA Comment Code: 6120

Comment: I would want to know drinking water was safe for my children and grandchildren. Wouldn't you?

Response: This is not a comment, a response is not necessary.

Commenter Name: M. Soule
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0381
EPA Comment ID: 19853
EPA Comment Code: 6120

Comment: No perchlorate in our drinking water!!! TOXIC AND HARMFUL!!!

Response: See response to comment code 6120.

Commenter Name: Edwards Mills
Commenter Organization: Kidem Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-0383
EPA Comment ID: 19854
EPA Comment Code: 6120

Comment: Please implement a meaningful standard for perchlorate.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0385
EPA Comment ID: 19855
EPA Comment Code: 6120

Comment: Set a Federal standard for perchlorate! Protect the public health!

Response: See response to comment code 6120.

Commenter Name: Brian Dewhirst, MD
Commenter Organization: Palmetto Primary Care Physicians
EPA Document ID: EPA-HQ-OW-2008-0692-0387
EPA Comment ID: 19856
EPA Comment Code: 6120

Comment: I am a family physician in South Carolina and take care of both adults and children. I want to express my deep concern about the EP's decision on addressing perchlorate in water. This chemical is known to be harmful and exposure through water could pose a serious danger to public health. Sincerely, Dr. Brian Dewhirst, MD Palmetto Primary Care Physicians Charleston, SC

Response: See response to comment code 6120.

Commenter Name: B. Meyer
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-0388
EPA Comment ID: 19857
EPA Comment Code: 6120

Comment: I am writing to support adding Perchlorate regulations under the Safe Water Drinking Act (Docket ID EPA-HQ-2008-0692) This chmeical, used in rocket fuel, is linked to thyroid problems in pregnant women, children and newborns. The EPA must regualte the chemical in drinking water.Millions are threatened, 16 million in 35 states. Protect our health.

Response: See response to comment code 6120.

Commenter Name: R. Sharp
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0391
EPA Comment ID: 19858
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPA's refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

This is a bad decision. Keep Perchlorate out of drinking water.

Response: See response to comment code 6120.

Commenter Name: D Camp
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0392
EPA Comment ID: 19859
EPA Comment Code: 6120

Comment: Water is more precious than gold, and highly needed healthy water for all living things. All the things found in surface water ends up in our bodies, so stop harmful chemicals in water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0393
EPA Comment ID: 19860
EPA Comment Code: 6120

Comment: Hypothyroidism is insidious and not diagnosed in time to avoid developmental deficiencies in children and dementia in old people.Perchlorate intake by children must be prevented at any cost. The standard for perchlorate in drinking water must be tightened.

Response: See response to comment code 6120.

Commenter Name: S. King

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0394
EPA Comment ID: 19861
EPA Comment Code: 6120

Comment: It is dangerous for the EPA to raise the amount of perchlorate allowed in public driking water. Keep the old standard and protect the health of U.S. citizens.

Response: See response to comment code 6120.

Commenter Name: M.M. Foxton
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0399
EPA Comment ID: 19862
EPA Comment Code: 6120

Comment: Please keep American drinking water safe.

Response: See response to comment code 6120.

Commenter Name: E. Heilman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0401
EPA Comment ID: 19863
EPA Comment Code: 6120

Comment: The EPA has a responsibility to protect the health of US citizens and is obligated to regulate and minimize the amount of perchlorate found in drinking water -- it is known to be harmful to pregnant women and children. Take responsibility now, do your job of protecting PEOPLE not companies, and regulate (minimize) the amount of perchlorate in American drinking water. Do the right thing.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0407
EPA Comment ID: 19864
EPA Comment Code: 6120

Comment: This is outrageous, I want to know that my drinking water is safe and free of anything harmful to my health. It's not acceptable to have unsafe levels of perchlorate in our drinking water.

Response: See response to comment code 6120.

Commenter Name: Tim Mathews
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0408

EPA Comment ID: 19865
EPA Comment Code: 6120

Comment: I strongly believe that the percholate levels in drinking water should be restricted much more conservatively.

Thank You,

Tim Mathews

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0409
EPA Comment ID: 19866
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPA's refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

At least six of my friends and family members have serious thyroid conditions, probably due to environmental exposures. This is epidemic, and it's no time to allow MORE perchlorate in drinking water, as it is something already known to help cause thyroid problems in pregnant women, newborns and young children.

You know how widespread perchlorate exposure is now in America. Setting a standard for it is a real step toward health risk reduction. Choosing not to regulate is choosing more disease, particularly for children.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0411
EPA Comment ID: 19867
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPA's refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

Perchlorate is a dangerous chemical that is currently found in the drinking water of 35 states. I urge you to set a standard for perchlorate in accordance with the Safe Drinking Water Act. Please protect American's health.

Response: See response to comment code 6120.

Commenter Name: Anonymous

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0412
EPA Comment ID: 19868
EPA Comment Code: 6120

Comment: Fresh, healthy and pure drinking water is a human right, whether or not a government agency wants to accept that fact. A human right! No single source should be able to alienate the people from that right. Therefor it is the obligation of those of power--whom the people have elected to represent them--to protect the rights of their constituents. Please do whatever you can to keep perchlorate as well as other toxic substances from the People's drinking water.

Response: See response to comment code 6120.

Commenter Name: K. Dalby
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0417
EPA Comment ID: 19869
EPA Comment Code: 6120

Comment: perchlorate is unsafe for consumption -- please keep out of drinking water!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0418
EPA Comment ID: 19870
EPA Comment Code: 6120

Comment: I am outraged to learn that while perchlorate has been detected in the water supplies of two-thirds of the states, there is no plan to create a minimum

acceptable level of this chemical.

Response: See response to comment code 6120.

Commenter Name: P. Incao
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0419
EPA Comment ID: 19871
EPA Comment Code: 6120

Comment: Perchlorate is a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children. Not regulating this harmful chemical in our drinking water is unacceptable.

Response: See response to comment code 6120.

Commenter Name: Masha Etkin MD, PhD
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0420
EPA Comment ID: 19872
EPA Comment Code: 6120

Comment: To EPA: Please regulate perchlorate in drinking water in accordance with the Save Drinking Water Act.

Thank you, Masha Etkin MD, PhD

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0425
EPA Comment ID: 19874
EPA Comment Code: 6120

Comment: I find it criminally obscene that there is no regulation of perchlorate in the water supply.

I find it convenient that the EPA has been repopulated with corporate advocates instead of those truly wishing to serve the public.

Response: See response to comment code 6120.

Commenter Name: E. Manire-Gatti
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0426
EPA Comment ID: 19875
EPA Comment Code: 6120

Comment: EPA must regulate the amount of perchlorate in drinking water so that it does not cause harm. Perchlorate is known to cause throid problems in pregnant women, newborns, and small children. This chemical can lead to delayed and altered development in children. It can lead to the development of tumors.

I understand that perchlorate is needed by the defense industry and its control will make its products more expensive. However, the health of the citizens of the United States is more important than spending more for weapons. Please remember our present and future generations when you consider the regulation of perchlorate.

Response: See response to comment code 6120.

Commenter Name: C. DiBenedetto
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0430
EPA Comment ID: 19876

EPA Comment Code: 6120

Comment: Please do not poison the people of America and our children. The EPA should regulate perchlorate in our drinking water, and the standards should not be lower than they are today -- they should be higher, if anything.

Response: See response to comment code 6120.

Commenter Name: Dorothea Leicher
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0431
EPA Comment ID: 19877
EPA Comment Code: 6120

Comment: This is written by Dorothea Leicher, at 2303 Delancey Pl, Philadelphia, PA, 19103, as a Public Comment regarding EPA's refusal to regulate Perchlorate under the Safe Water Drinking Act (Docker ID EPA-HQ-OW-2008-0692)

Perchlorate has been linked to thyroid problems in pregnant women, newborns and young children. As mother, this kind of risk to my daughter and her children is of great concern.

Perchlorate is found in the drinking water of 35 states, so that regulating it would provide a significant protection for the public.

Safe drinking water is an extremely important asset, and one that we will have to rely on increasingly as water becomes scarcer. the trust in tap water has already been assaulted by the bottled water industry and it is especially important now do everything to protect this public resource in the spirit of the Safe Water Drinking Act. Thank you for your time and attention.

Response: See response to comment code 6120.

Commenter Name: S. Carr
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0435
EPA Comment ID: 19880
EPA Comment Code: 6120

Comment: Perchlorate toxicity is proven beyond doubt. Why is there a question about its' regulation? It is ridiculous to poison people on purpose although the U.S. chemical industry has been doing so for half a century. Most of the cancers, thyroid problems, and birth defects seem related to the chemical industry and the lack of proper regulation from the EPA. If the EPA cannot do better, they should start over with a new agency that can protect us and close this one down.

Response: See response to comment code 6120.

Commenter Name: B. Welsh
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0438

EPA Comment ID: 19881
EPA Comment Code: 6120

Comment: Do not allow more Perchlorate in our drinking water! Our water continues to degrade in quality - in part by various pollutants which are virtually impossible to study in the combinations they'll actually appear in. These combinations are virtually impossible to study due to their large numbers, but evidence so far indicates that the total effect of these pollutants is worse than the sum of effects of the separate pollutants.

Clean water is critical for life - and it's far cheaper and more sensible to keep the water clean rather than to clean it up after it's polluted.

Response: See response to comment code 6120.

Commenter Name: G. Miller
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0442
EPA Comment ID: 19882
EPA Comment Code: 6120

Comment: I don't think any substance should be in our drinking water, except what our Creator put there. As far as any perchlorate is concerned, they don't belong in our water supply. If there is no way to eradicate it, then it should be the smallest amount possible. This seems like something the EPA should know without our input. There our so many diseases now that I feel are caused by the chemicals in our atmosphere; consequently, we don't want to allow this chemical in our water supply, which would endanger the health of our citizens.

I strongly urge the EPA to set a high standard for our drinking water.

Response: See response to comment code 6120.

Commenter Name: J. Rinker
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0444
EPA Comment ID: 19883
EPA Comment Code: 6120

Comment: Perchlorate has a long history of use in rocket fuel and its has been shown to disrupt iodine uptake, which can lead to endocrine abnormalities in our most susceptible populations including pregnant women, newborns and small children.

Given that it has been found in the drinking water of 35 states in the US, it is imperative that the EPA not only regularly review but regulate this chemical to protect our families and future heritage.

As an occupational and environmental medicine physician I strongly urge that the EPA set a standard for perchlorate in our drinking water in order to protect American's health. Don't lose this opportunity to set regulations for reducing our health risks from chemically contaminated drinking water in accordance with the Safe Drinking Water Act.

Response: See response to comment code 6120.

Commenter Name: A. R. Ehrlich, MD
Commenter Organization: Group Health Cooperative Health Care
EPA Document ID: EPA-HQ-OW-2008-0692-0445
EPA Comment ID: 19886
EPA Comment Code: 6120

Comment: Perchlorate in drinking water should be limited. I understand that thus far the EPA has refused to do this, which puts millions of small children and pregnant women at risk from the harmful effects on the thyroid.

A R Ehrlich, MD

Response: See response to comment code 6120.

Commenter Name: Jeoffry B. Gordon, MD, MPH
Commenter Organization: Ocean Beach Medical Group
EPA Document ID: EPA-HQ-OW-2008-0692-0448
EPA Comment ID: 19887
EPA Comment Code: 6120

Comment: As apractici8ng physician with a devotion to environmental health diseases, it is my opinion that the preponderance of the available evidence would indicate that it is important to have a margin of safety by reducing the proposed level of perchlorate in drinking water by a factor of 20.

Response: See response to comment code 6120.

Commenter Name: Ellen M. Imbody
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0450
EPA Comment ID: 19888
EPA Comment Code: 6120

Comment: As a retired public health comissioner, I urge you to regulate the Perchlorate which is now found in the drinking water in 35 states. Percholate is a dangerous chemical. Without regulation too many Americans risk being exposed to this

chemical. With control of this chemical, you will be protecting our citizens health.

Sincerely,

Ellen M. Imbody Pinetop, AZ

Response: See response to comment code 6120.

Commenter Name: B. Regulinski

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0451
EPA Comment ID: 19889
EPA Comment Code: 6120

Comment: The EPA needs to set a maximum level of pechlorate in drinking water. AS FAR AS I AM CONCERNED THERE IS NO SAFE LEVEL FOR FOREIGN CHEMICALS IN DRINKING WATER. There is already a shortage of clean drinking water in the world. Water is essential to life, and I resent the contamination of the little that the world has. Many wells in my area of Arizona have had to be closed because of chemicals from cleaning air plane engines and manufacture of computer chips.

There is no excuse for allowing manufacturers to dump their waste water into the supply of clean drinking water.

Response: See response to comment code 6120.

Commenter Name: R. Sheridan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0452
EPA Comment ID: 19890
EPA Comment Code: 6120

Comment: I would like to comment regarding EPA's refusal to regulate Perchlorate under the Safe Drinking Act (Docket ID EPA-HQ-OW-2008-0692.

I think perchlorate should be regulated because it is a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children. This harmful chemical should be regulated. It has been found in Alaska, as well as in 34 other states. According to the EPA's data it has been shown that we are at risk of being exposed to this chemical.

I urge you to set a standard for perchlorate in accordance with the Safe Drinking Water Act.

Ruth Sheridan, Anchorage, AK

Response: See response to comment code 6120.

Commenter Name: Catherine Moore
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0453
EPA Comment ID: 19891
EPA Comment Code: 6120

Comment: Perchlorate is not something I can drink safely. I already have a huge problem with my thyroid which can cause heart failure and a number of other serious problems. Please find a way to monitor and clean up this toxic material which is finding its way into our drinking water.

Many thanks, Catherine Moore, Oregon

Response: See response to comment code 6120.

Commenter Name: Grace Goldberg, DO
Commenter Organization: MidCoast Maine Cares (MCMC)
EPA Document ID: EPA-HQ-OW-2008-0692-0457
EPA Comment ID: 19892
EPA Comment Code: 6120

Comment: Please remember that you are the Environmental Protection Agency. Please do not raise the acceptable level of perchlorates in drinking water. Thankyou

Response: See response to comment code 6120.

Commenter Name: David P. Kuter, M.D.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0458
EPA Comment ID: 19893
EPA Comment Code: 6120

Comment: As a physician, I have reviewed the evidence and believe that more stringent guidelines are wise for the presence of perchlorate in water supplies.

David P. Kuter, MD 3917 Regent Street, Madison, WI 53705

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0467
EPA Comment ID: 19896
EPA Comment Code: 6120

Comment: Protect our nation's drinking water for rocket fuel, protect the health interests of pregnant women and children.

Response: See response to comment code 6120.

Commenter Name: N. O'Byrne
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0468
EPA Comment ID: 19897
EPA Comment Code: 6120

Comment: We must regulate perchlorate in our drinking water to an acceptable standard that does not endanger public health.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0471
EPA Comment ID: 19900
EPA Comment Code: 6120

Comment: regulate perchlorate to the old standands.

Response: See response to comment code 6120.

Commenter Name: James R. and Mary Duplisea Palmer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0472
EPA Comment ID: 19901
EPA Comment Code: 6120

Comment: My wife (Mary Duplisea-Palmer) and I (James R. Palmer) live at 66 Albert Pt. in Stetson, ME. This is our public comment regarding EPA's refusal to regulate Perchlorate under the Safe Drinking Water Act: Please continue to regulate this chemical according to the standard that was in place before this proposed change. Clean drinking water is so important to life, and, unfortunately, humankind has pollutted it too much already. Even using EPA's data, this chemical is wide-spread already. Continue to do the job your agency was created to do.

Response: Perchlorate is not regulated in drinking water. See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0475
EPA Comment ID: 19902
EPA Comment Code: 6120

Comment: The Environmental Protection Agency has formally refused to set a drinking-water standard for perchlorate, a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0475
EPA Comment ID: 19904
EPA Comment Code: 6120

Comment: Is there something wrong with this picture? Why not help as an agency to be part of the Green Revolution by advocating for an entire network of workers whose sole goal would be to screen out (phase out) every iota of perchlorate from our drinking supply? And let's get more honest about flouride, too.

Response: See response to comment code 6120. The comment about flouride is outside the scope of this notice; no response is necessary.

Commenter Name: Melvyn C. Thorne
Commenter Organization: Johns Hopkins University
EPA Document ID: EPA-HQ-OW-2008-0692-0482
EPA Comment ID: 19905
EPA Comment Code: 6120

Comment: The regulatory limits on perchlorate in drinking water have been set irresponsibly too high. This is yet another of the reckless endangerments of public health produced by the Bush administration to pander to an unbalanced ideology of deregulation of industry.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0483
EPA Comment ID: 19906
EPA Comment Code: 6120

Comment: Please, please, please put our health and welfare first. No perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: O. Yourke
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0485
EPA Comment ID: 19907
EPA Comment Code: 6120

Comment: I think this decision is harmful to public health. No perchlorate should b allowed in drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0486
EPA Comment ID: 19908
EPA Comment Code: 6120

Comment: Regulate percholate in all of our nations water supply. Do your job and protect the environment.

Response: See response to comment code 6120.

Commenter Name: Dave Weller, MPH
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0487
EPA Comment ID: 19909
EPA Comment Code: 6120

Comment: EPA staffers,

Please demand that all industrial chemicals be removed from our drinking water supply. Your current work in regulating perchlorate is especially important. Remove them from our water.

Thank you, Dave Weller (MPH)

Response: See response to comment code 6120. The comment about other industrial chemicals is outside the scope of this notice; no response necessary.

Commenter Name: S. G. Gompf
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0490
EPA Comment ID: 19910
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPAâ€™s refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

Perchlorate is component of rocket fuel. It has been linked to thyroid disease in pregnant women, in newborns and young children. It is incomprehensible, and indefensible, that the EPA has refused to regulate a dangerous chemical in the drinking water of American mothers and children.

Response: See response to comment code 6120.

Commenter Name: C. Gabriel
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0492
EPA Comment ID: 19913
EPA Comment Code: 6120

Comment: Perchlorate is a known health hazard. The EPA's refusal to set standards for it is unconscionable, and an abrogation of it's charter.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0493
EPA Comment ID: 19914
EPA Comment Code: 6120

Comment: Public Comment Regarding Immediate need to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

As an physician and a mother I am quite concerned about the lack of regulation of Perchlorate, a chemical in rocket fuel, linked to thyroid problems in pregnant women, newborns and young children let alone other as of yet undetermined consequences.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0493
EPA Comment ID: 19916
EPA Comment Code: 6120

Comment: Please use foresight and help to protect our drinking water by setting a standard for perchlorate.

Response: See response to comment code 6120.

Commenter Name: Jan L. Crean, M.D.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0494
EPA Comment ID: 19917
EPA Comment Code: 6120

Comment: I am writing to urge the EPA to control the contamination of our drinking water and, by extension, our food supply with regard to perchlorate. The following is medical information regarding this toxic chemical, per the EPA itself:

PERCHLORATE

The EPA has established an official reference dose (RfD) of 0.0007 mg/kg/day of perchlorate. This level is consistent with the recommended reference dose included in the National Academy of Science's January 2005 report. A reference dose is a scientific estimate of a daily exposure level that is not expected to cause adverse health effects in humans. Risk information about perchlorate and perchlorate salt.

Perchlorate is a man-made anion commonly associated with the solid salts of ammonium, potassium, and sodium. Ammonium perchlorate is the mostly widely used perchlorate compound. It has also been found to occur naturally in certain highly arid environments. These salts are highly soluble in water, and because perchlorate adheres poorly to mineral surfaces and organic material, it can be very mobile in surface and subsurface aqueous systems. Also, since it is relatively inert in typical groundwater and surface water conditions, perchlorate contamination may persist for extended periods of time.

Perchlorate interferes with iodide uptake into the thyroid gland. Because iodide is an essential component of thyroid hormones, perchlorate disrupts how the thyroid functions. In adults, the

thyroid helps to regulate the metabolism. In children, the thyroid plays a major role in proper development, in addition to metabolism. Impairment of thyroid function in pregnant mothers may impact the fetus and result in such effects as changes in behavior, delayed development and decreased learning capability. Drinking water contaminated with perchlorate is the most likely way that perchlorate can be ingested.

Recent studies conducted by the U.S. Department of Agriculture (Nov. 2004) and the Environmental Working Group (Apr. 2003) have detected perchlorate in samples of lettuce in California. Several other studies also detected perchlorate in milk samples taken from California and Texas. Additional studies of perchlorate uptake in food crops are currently being conducted by the U.S. Food and Drug Administration.

Production of ammonium perchlorate first began in the United States in the mid- 1940s, primarily for use by the U.S. military. The most common uses for ammonium perchlorate are in explosives and rocket propellants, which have been widely used in military munitions items, such as mortars, grenades and flares and solid fuel rocket. Based on production data from two perchlorate manufacturers, it is estimated that 90 percent of perchlorate compounds are manufactured for use in defense activities and the aerospace industry. While occurring most frequently at domestic Air Force installations, ammonium perchlorate has been detected at Army and Navy sites too. The National Aeronautics and Space Administration (NASA) and Department of Energy (DOE) also have a small number of facilities with perchlorate (specific information on known perchlorate releases in the U.S. (XLS) (PDF, 7 pages, 515KB), as of September 23, 2004). In addition, ammonium perchlorate and the other perchlorate salts have been or are used in a wide range of applications, including pyrotechnics and fireworks, blasting agents, solid rocket fuel, matches, lubricating oils, nuclear reactors, air bags and certain types of fertilizers. Improper storage and/or disposal related to the uses mentioned above are the most typical route for perchlorate to enter into the environment.

The EPA has been working with states, federal agencies, tribes, water suppliers and the private sector for several years to address perchlorate. In 1998, EPA released an Interim Assessment Guidance for Perchlorate (PDF, 4 pages, 224KB), which was then subject to peer review in 1999. The external review draft of the revised document "Perchlorate Environmental Contamination: Toxicological Review and Risk Characterization," (November, 2002) responds to those recommendations emanating from the peer review.

The National Research Council of the National Academies published its technical review of the Health Implications of Perchlorate Ingestion in January 2005. From this review, EPA has established an official reference dose of 0.0007 mg/kg/day of perchlorate. This level is consistent with the recommended reference dose included in the National Academy of Science's report. A reference dose is a scientific estimate of a daily exposure level that is not expected to cause adverse health effects in humans.

Thank you for your attention to this matter. As a practicing OB/Gyn, I am intimately concerned with your actions, on behalf of my patients and their children, both born and unborn.

Response: See response to comment code 6120.

Commenter Name: Richard F. Koch
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-0495
EPA Comment ID: 19918
EPA Comment Code: 6120

Comment: This is a public comment on the matter of perchlorate content of drinking water.

I urge that the standard be returned at least to the level permitted by today's standard. Better yet, a lower level should be mandated.

Richard F. Koch dickkoch88@gmail.com

Response: EPA does not regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Alison M. Russell
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0498
EPA Comment ID: 19919
EPA Comment Code: 6120

Comment: As a private citizen who also works in the water field, I urge you to adopt a strict health standard for the regulation of perchlorate in drinking water. No water consumer should have to bear the furden of any of this chemical in their water.

Thank you.

Alison M. Russell 548 Sumner St. Santa Cruz, CA 95062

Response: See response to comment code 6120.

Commenter Name: Sister Mary Schmuck
Commenter Organization: Sisters of Mercy
EPA Document ID: EPA-HQ-OW-2008-0692-0499
EPA Comment ID: 19920
EPA Comment Code: 6120

Comment: Letting perchlorate into water is very harmful to human health.

Please prohibit it!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0501
EPA Comment ID: 19921
EPA Comment Code: 6120

Comment: PERCHLORATES DAMAGE HEALTH IN ALL SENTIENT BEINGS!!! (THAT INCLUDES 'YOU' WAY PAST TIME TO INSTITUTE 'SAFE' LIMITS (I.E. NONE!) AS IT IS IN OUR WATER SUPPLY AND AFFECTS EVERYTHING, GRAZING GRASSES, FOODS, AND EVEN SHOWS UP IN OUR MILK PRODUCTS!!!

MY UNDERSTANDING IS THAT THE EPA IS 'SUPPOSED' TO KEEP TRACK OF SAFE LIMITS OF BAD CHEMICALS AND MANDATE THAT THESE LIMITS ARE ACTUALLY ENFORCED.

TIME TO DO YOUR JOB..... YOUR BAD, LACK OF CONTROL, IS KILLING ALL THINGS.

Response: See response to comment code 6120.

Commenter Name: Dr. L. Paull
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0502
EPA Comment ID: 19922
EPA Comment Code: 6120

Comment: The current levels of perchlorate idrinking water are alarmingly dangerous. The EPA must regulateee the practices that are creating this level.

Response: See response to comment code 6120.

Commenter Name: L. Peles, M.D.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0503
EPA Comment ID: 19923
EPA Comment Code: 6120

Comment: I think this is dangerous to our health.

Response: This is not a comment, a response is not necessary.

Commenter Name: Rhea Irvine
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0504
EPA Comment ID: 19924
EPA Comment Code: 6120

Comment: It's more than a shame that citizens of many European countries are protected from substances that *may* endanger health than citizens of our own country. Among the many things that have declined under the current Republican administration, health and environmental protections --and the ethics of protecting or not protecting---rank high. Clean air and clean water should not be things that need to be debated or lobbied for. I urge you to set standards for perchlorate in water that are supported by the best scientific research.

Thank you, Rhea Irvine

Response: See response to comment code 6120.

Commenter Name: Kristen E. Cain
Commenter Organization: FACOG
EPA Document ID: EPA-HQ-OW-2008-0692-0505
EPA Comment ID: 19925
EPA Comment Code: 6120

Comment: As a physician specializing in hormonal disorders, I cannot understand how this benefits any Americans. This compound may be linked to breast, ovarian, uterine, testicular and prostate cancers as well as infertility, birth defects, and is a documented offender in thyroid disease. Allowing an increase in levels of perchlorate in our tap water will increase disease, health care costs, usage of bottled water, energy costs for transport of bottled water and petroleum byproduct usage for the bottling of the water in a public attempt to avoid exposure to these pollutants. We need to be making our water safer! Kristen E. Cain, MD, FACOG

Response: See response to comment code 6120.

Commenter Name: J. Angelina
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0507
EPA Comment ID: 19927
EPA Comment Code: 6120

Comment: I believe this is dangerous to the public safety!

Response: See response to comment code 6120.

Commenter Name: Noel Rasor
Commenter Organization: MUP
EPA Document ID: EPA-HQ-OW-2008-0692-0508
EPA Comment ID: 19928
EPA Comment Code: 6120

Comment: I urge the EPA to return to limit perchlorate levels in drinking water to its own 2002 recommendations on what can be considered safe. This chemical is known to be harmful and exposure through water could pose a serious danger to public health. Sincerely, Noel Rasor, MUP

Response: See response to comment code 6120.

Commenter Name: J. McPeek
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0510
EPA Comment ID: 19929
EPA Comment Code: 6120

Comment: Rocket fuel or anything like it in my tap water does nothing to enhance my health, and could damage it. Safe level my rear end! There is no such thing.

Response: See response to comment code 6120.

Commenter Name: Christine Lomaka
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0512
EPA Comment ID: 19930
EPA Comment Code: 6120

Comment: Hi. I am a citizen of Portland, Maine. I have learned of your determination to not regulate perchlorate in our drinking water, though the amount of perchlorate in our water has been on the rise. It has been found to cause thyroid problems in pregnant women and in the youth of our country. These are among the very people this department has been created to protect. You should not support businesses at the expense of the people's and the environment's health. Do your job for the effects are lasting.

Sincerely, Christine Lomaka CLonthroad@aol.com 76 Monument St. Portland, ME 04101

Response: See response to comment code 6120.

Commenter Name: C. Steinberg
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0513
EPA Comment ID: 19931
EPA Comment Code: 6120

Comment: This is to support the positon of Physicians for Social Responsibility on the matter of minimum perchlorate residue in drinking water. I can't understand why EPA is backtracking on its minimum set years ago, proposing to more than double that minimum. In that major industrialized nations have perchlorate minima in drinking water even lower than the former EPA minimum, are we in this country reverting to the safety gauges more consistent with those in some non-industrialized lands? The proposed elevation of the perchlorate minima for our drinking water is disgraceful.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0515
EPA Comment ID: 19932
EPA Comment Code: 6120

Comment: The function of the EPA is to promote health for the citizens of the United States as well as the natural environment within the national borders. I am informed that the EPA's current acceptable minimum for perchlorate is 15 times the level that had been set in 2002. This is unacceptable, as scientific research has indicated the dangerous effects of perchlorate on pregnant

women, new born and young children. I urge you to set a lower, mandatory safe minimum for perchlorate, because it should not be a part of our drinking water.

Response: See response to comment code 6120.

Commenter Name: T. Udall
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0516
EPA Comment ID: 19933
EPA Comment Code: 6120

Comment: Allowing perchlorate in drinking water is akin to murder, slow and torturous death, with or without healthcare. Corporations who think they are superior to life or that they have the right to destroy life without legal consequences must be regulated or there will come a time when there is no life left.

Response: This is not a comment, a response is not necessary.

Commenter Name: H. Meyer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0517
EPA Comment ID: 19934
EPA Comment Code: 6120

Comment: Perchlorate in our drinking water is harmful. Our limit should be none allowed. This chemical has been shown to be dangerous to infants and children causing thyroid disease, which may be a lifelong problem costing the individuals to suffer increased insurance fees, medication costs and problems with schooling. As a pediatrician I am appalled that the EPA has allowed an increase in the water levels of perchlorate a most dangerous substance.

Response: See response to comment code 6120.

Commenter Name: T. Johnson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0518
EPA Comment ID: 19935
EPA Comment Code: 6120

Comment: This is found in Rocket Fuel people, ROCKET FUEL! Hello-this should be stopped NOW. Your actions affect the lives of people, their health and well being.

This should not be allowed and the EPA has the power to stop this nonsense.

So STOP allowing this in our drinking water!

Response: See response to comment code 6120.

Commenter Name: Anonymous

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0521
EPA Comment ID: 19936
EPA Comment Code: 6120

Comment: No individual anywhere has been given the right to poison our drinking water and food. Any individual or agent who willfully poisons our water is a criminal. Do no poison our water with poisons, inorganic or viral. You are not protecting our health or the environment by poisoning our water with deadly toxins.

Response: This is not a comment, a response is not necessary.

Commenter Name: Joyce Paape
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0524
EPA Comment ID: 19937
EPA Comment Code: 6120

Comment: Do not raise the amount of percolate in our drinking water- it would endanger more people than the present levels- especially pregnant wome & children!! Dr. Joyce Paape

Response: Perchlorate is not regulated in drinking water. See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0527
EPA Comment ID: 19939
EPA Comment Code: 6120

Comment: I believe that in this country we should be able to depend on our drinking water being safe, the air we breathe, the food we eat. What is the problem that you people cannot insure that that happens in this country?

Response: This is not a comment, a response is not necessary.

Commenter Name: Jana Koth
Commenter Organization: UNMC
EPA Document ID: EPA-HQ-OW-2008-0692-0528
EPA Comment ID: 19940
EPA Comment Code: 6120

Comment: Perchlorate is hazardous and needs to be eliminated. This is a dangerous public health concern.

Response: This is not a comment, a response is not necessary.

Commenter Name: M. Huber
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-0529
EPA Comment ID: 19941
EPA Comment Code: 6120

Comment: Drinking water is valuable and increasingly scarce. Please keep our free of chemicals.

Response: See response to comment code 6120.

Commenter Name: Rebecca Fletcher
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0530
EPA Comment ID: 19942
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPAâ€™s refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

I'm very concerned about this. Please regulate the quantities of this dangerous chemical that are allowed to be present in drinking water. I know that perchlorate is a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children. Not regulating this harmful chemical in our drinking water is totally unacceptable. Perchlorate is found in drinking water in 35 states, and according to the EPAâ€™s own data, 16 million Americans are at risk of being exposed to this dangerous chemical.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0533
EPA Comment ID: 19944
EPA Comment Code: 6120

Comment: Set a drinking water standard for Perchlorate.

It's absurd for the EPA to refuse to set standards for this harmful pollutant in drinking water.

It's the same as not regulating the amount of lead or mercury allowed in public drinking water.

Do your job EPA. Protect the environment, protect the people. Set a rigorous standard for Perchlorate in drinking water!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0534
EPA Comment ID: 19945
EPA Comment Code: 6120

Comment: I believe perchlorate is harmful to the public health. It causes thyroid problems in pregnant woman, newborns, and young children. Moreover, the safe limit for perchlorate is 15 times greater than what EPA declared in 2002. Too many people are potentialy exposed to this dangerous toxin.

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0536
EPA Comment ID: 19946
EPA Comment Code: 6120

Comment: why on earth would you add harmful chemicals to our drinking water!?!!!

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0540
EPA Comment ID: 19947
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPA's refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

The high level of perchlorate allowed in our current drinking water supply is shameful and unethical. Our government is the ONLY party that has the authority to regulate toxic industrial emissions in our environment, and yet our government continues to protect industry rather than people.

Please keep the health of ordinary americans safe. Please pass legislation that requires cities and industries to clean up contaminated water to stricter standards. The technology exists today to do this! Why is this not happening?

I urge you to create the strictest possible standards of perchlorate in our drinking water to keep future generations safe and healthy, in accordance with the Safe Drinking Water Act.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0541
EPA Comment ID: 19948
EPA Comment Code: 6120

Comment: Allowing perchlorate in drinking water is a health risk! This decision is hazardous to the American population.

Response: See response to comment code 6120.

Commenter Name: L. Abbott
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0542
EPA Comment ID: 19949
EPA Comment Code: 6120

Comment: As perchlorate is detected in municipal water systems we need a strict standard to safeguard the public. We must always ere on the side of safety.

Response: See response to comment code 6120.

Commenter Name: Karen Ulring
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0543
EPA Comment ID: 19950
EPA Comment Code: 6120

Comment: The EPA must set a standard that regulates the amount of perchlorate in our drinking water. It s well documented that this chemical in our water is dangerous, especially to pregnant women, and to peoples health in general. Please act to ensure the health of US citizens.

Thank you, Karen Ulring

Response: See response to comment code 6120.

Commenter Name: C.M. Adams
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0545
EPA Comment ID: 19951
EPA Comment Code: 6120

Comment: I am VERY sure that the United States needs very specific regulations on the amount of perchlorate allowed in public drinking water. Strict Regulations.

The American public expect to be protected by the EPA and their government, not subject to policies that make it easy for pollution to remain in their

water and polluters to go unpunished. We need to change jet fuel if it pollutes water sources.

Do not let Americans down by allowing pollution that may cause Thyriod problems to remain in our water. There are at least 5 people i can name who have thryriod issues, many living in our tiny little town that is too small to have a post office.

my husband was diagnosed 2 months ago.

This is a VERY serious issue. Do not allow corporations to continue as they are, just because it's easy to avoid rocking the boat.

Thank you for your time and attention to this matter.

Response: See response to comment code 6120.

Commenter Name: Kenneth A. Popio
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0547
EPA Comment ID: 19952
EPA Comment Code: 6120

Comment: I think making levels of allowable perchlorate in drinking water is hazardous to public health.

Kenneth A. Popio

Response: See response to comment code 6120.

Commenter Name: M. O'Brien
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0548
EPA Comment ID: 19953
EPA Comment Code: 6120

Comment: Perchlorate in their drinking water exposes 20 to 40 million Americans to the unnecessary risk of thyroid problems, according to independent analysis. Please see to it that the levels considered allowable are reduced significantly and monitored. Refusing to regulate the chemical ignores a significant harm to public health.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0549
EPA Comment ID: 19954
EPA Comment Code: 6120

Comment: As a Registered Nurse, I am sickened by the lack of protection of our water supply when it comes to contaminants such as perchlorate. We know, beyond doubt, that there is no safe limit of this chemical in water. We must demand that our government do what is right and protect unsuspecting citizens from chemicals that are pervasive in our environment.

Response: This is not a comment, a response is not necessary.

Commenter Name: T. C. Washburn
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-0550
EPA Comment ID: 19955
EPA Comment Code: 6120

Comment: As a public health physician and a Pediatrician, I am very concerned about potential hazards of perchlorate in drinking water. There appears to be ample evidence of potential thyroid disease in newborns and young children.

Please strongly consider setting a standard for maximal allowable perchlorate levels in drinking water.

Thank you for your consideration.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0554
EPA Comment ID: 19956
EPA Comment Code: 6120

Comment: please eliminate/ limit perchlorate from our drinking water.

Response: See response to comment code 6120.

Commenter Name: D. Burton
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0555
EPA Comment ID: 19957
EPA Comment Code: 6120

Comment: Please reevaluate your decision on perchlorate residue in drinking water. Our children need protection from a lifetime of such chemicals when possible.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0559
EPA Comment ID: 19958
EPA Comment Code: 6120

Comment: Even if the perchlorate itself posed no apparent harm, which I believe it does, there have been no adequate studies of how iut interacts with othere chemicals or how sensitive individuals react to it. Additionally, how can the EPA or any group force American citizens to expose themselves to chemicals they believe they should not have in their systems?

Response: This is not a comment, a response is not necessary.

Commenter Name: L. Garvey
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0571
EPA Comment ID: 19959
EPA Comment Code: 6120

Comment: Nix Perchlorate! Do your job-Protect our water & health! You work for citizens, not industry! Discusted!

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0574
EPA Comment ID: 19960
EPA Comment Code: 6120

Comment: Given a pattern in recent years of the FDA caving in to pressures from an administration that is militantly anitscience (and pro-corporate profits), I do not trust that a relaxing of regulation of perchlorate is in the public's best interest.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0575
EPA Comment ID: 19961
EPA Comment Code: 6120

Comment: It is the mandate of the Environmental Protection Agency to protect U.S. residents from agents in our environment that are, or are potentially, harmful to our health. I thoroughly disagree with the proposal to stop regulating perchlorate in our water supply.

Response: See response to comment code 6120.

Commenter Name: David Myers
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0577
EPA Comment ID: 19962
EPA Comment Code: 6120

Comment: Do not compromise the acceptable level of perchorate in drinking water. Drinking water standards should not exceed levels determined safe in your own study of 2002. Keep our water safe.

Thank you.

David Myers

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0579
EPA Comment ID: 19963
EPA Comment Code: 6120

Comment: It is not safe that perchlorate in the drinking water is fit to drink.

Response: See response to comment code 6120.

Commenter Name: Karl J. Volk
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0582
EPA Comment ID: 19965
EPA Comment Code: 6120

Comment: I Karl J.Volk of 43 whittier blvd declare the EPA as not doing its job of protecing me against environmental issues in general and specifically against Perchlorate and "allowable " Levels . You are gettingmy Tax dollars andI want you to set limits on the prnicious fuel in the water aquivers. Shame on you God dam it

Karl J.Volk

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0583
EPA Comment ID: 19966
EPA Comment Code: 6120

Comment: Perchlorate is detrimental to human health. In particular, it disturbs thyroid functioning which in turn compromises immune functioning. It has been discovered to be present in the drinking water in at least 35 states. For these reasons, it must be declared hazardous and regulated.

Response: See response to comment code 6120.

Commenter Name: E.L. Blair
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0584
EPA Comment ID: 19967
EPA Comment Code: 6120

Comment: I am writing to express my anger over the plan for the EPA not to regulate perchlorate in drinking water even though it has been found in water in 35 states. What part of Environmental PROTECTION do you not understand?

I would like to see the EPA do what it is mandated to do by regulating perchlorate. This is nothing but a give-away to the weapons-making industries.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0586
EPA Comment ID: 19969
EPA Comment Code: 6120

Comment: Is it not enough that the Senate Environment and Public Works Committee has endorsed legislation requiring the EPA to set a federal standard for perchlorate and to monitor levels of Perchlorate in tap water? The American public deserves to be able to drink their water with confidence that it's safe. If it isn't we may as well move to some third world country where the first question is, "Can I drink the water?" For shame, EPA!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0592
EPA Comment ID: 19970
EPA Comment Code: 6120

Comment: Please stop poisoning the earth and all its inhabitants with your thirst for war profits. Stop building rockets and start saving lives.

Response: This is not a comment, a response is not necessary.

Commenter Name: Mary Sue Penn
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0601
EPA Comment ID: 19972
EPA Comment Code: 6120

Comment: Please do not loosen standards for perchlorate. Our tap water is polluted enough! Go back at least to 2002 standards! We want pure, clean water.

Thank you, Mary Sue Penn

Response: See response to comment code 6120.

Commenter Name: G. Grant

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0609
EPA Comment ID: 19973
EPA Comment Code: 6120

Comment: I am writing to express my concern regarding the EPA's failure to regulate perchorate, as well as the proposed reference level. The citizens of the USA neeed their health protected from this toxin in our water. The health of our children need this protection. Thyroid disease has become too common and this autoimmune disease affects ones entire health. It is not a simple disease. It is not diaganosed and controlled easily as some seem to think. I request that the EPA take time for a complete and through evaluation, review the ever-changing scientific findings permitting the community time to evaluate and comment on the findings. Please do not rush a decision, one that could adversily affect the women and children of this great nation.

Response: See response to comment code 6120.

Commenter Name: L. Skipper
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0611
EPA Comment ID: 19974
EPA Comment Code: 6120

Comment: I would like to comment regarding the EPA's failure to regulate perchlorate in the drinking water. It can cause thyroid problems. Five years ago, I was diagnosed as hypothyroid and my life has been ruined since then. The thought of this happening to millions of other people because the government has decided to look the other way in safeguarding our drinking water is outrageous! We depend on the EPA to protect the public and require the strongest standards for our drinking water. The public is looking for high standards for their drinking water without perchlorate in it.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0623
EPA Comment ID: 19975
EPA Comment Code: 6120

Comment: Given the nature of the epidemic of thyroid dysfunction, and the increased health cost of treatment of such dysfunction, it is essential to set new, regulatory levels of Perchlorate in Drinking water to absolute lowest levels, with intention to eliminate sources of additional contamination in an urgent and immediate timely approach to safeguard further risk to public exposure.

Further, all public schools must be equipped with appropriate filters on drinking water taps immediately.

Further, all public facilities = hospitals, restaurants, should be strongly advised to obtain, through tax relief measures, safe and reliable filters for all tap water sources.

The public has the right to be protected. The cost of prevention far out weighs the cost of treatment.

Response: See response to comment code 6120.

Commenter Name: Margaret Baco
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0624
EPA Comment ID: 19976
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPAâ€™s refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

Perchlorate is a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children. Not regulating this harmful chemical in our drinking water is unacceptable.

Perchlorate is found in drinking water in 35 states, and according to the EPAâ€™s own data, 16 million Americans are at risk of being exposed to this dangerous chemical. The cost of treating this epidemic of thyroid dysfunction is beyond estimate.

Response: See response to comment code 6120.

Commenter Name: Judith DiBiase Bennis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0631
EPA Comment ID: 19981
EPA Comment Code: 6120

Comment: PLEASE ban perchlorate from our environment, especially water resources. The EPA must set very high regulation standards for this chemical that is poisoning our children, and in my case, grandchildren.

Thank you.

Juidth DiBiase Bennis 32 Summit Pass Medford, NJ 08055

Response: See response to comment code 6120.

Commenter Name: Carole
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0632
EPA Comment ID: 19982
EPA Comment Code: 6120

Comment: Do not allow approve or in any way havepercholate in any waters that we ultimately will drink

Response: See response to comment code 6120.

Commenter Name: L.A. Coons
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0644
EPA Comment ID: 19986
EPA Comment Code: 6120

Comment: Perchlorate in our drinking water is not safe! Do your job and protect the public. -Lisa A. Coons

Response: See response to comment code 6120.

Commenter Name: L. Segnitz
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0645
EPA Comment ID: 19987
EPA Comment Code: 6120

Comment: as a physician, i ask you to please strongly consider regulating and monitoring perchlorate in tap water. there are significant health consequences of ingestion of this chemical. thank you.

Response: See response to comment code 6120.

Commenter Name: K. Peterson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0646
EPA Comment ID: 19988
EPA Comment Code: 6120

Comment: I am appalled that the Environmental Protection Agency (EPA) has formally refused to set a drinking-water standard for perchlorate, a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children.

Response: See response to comment code 6120.

Commenter Name: K. Peterson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0646
EPA Comment ID: 19990
EPA Comment Code: 6120

Comment: Under this new standard, more than 16 million Americans are exposed to unsafe levels of perchlorate in their drinking water, and independent analysis shows anywhere from 20 to 40 million Americans at risk. Perchlorate has been found in the drinking water in 35 states in the U.S. We should be working to protect our water and our environment; the fact that you are even considering raising these levels is unbelievable.

We cannot continue to pollute our tap water. Besides the fact that this is bad for the environment, (the entity that your agency is supposed to protect), this is becoming social justice issue as well.

Response: This is not a comment, a response is not necessary.

Commenter Name: Luis Olmedo Vélez
Commenter Organization: omité Cívico del Valle, Inc.
EPA Document ID: EPA-HQ-OW-2008-0692-0652
EPA Comment ID: 19993
EPA Comment Code: 6120

Comment: Luis Olmedo Vélez Executive Director Comité Cívico del Valle, Inc. 699 E Street Brawley, CA 92227 October 24, 2008

Eric Burneson Office of Ground Water and Drinking Water Standards and Risk Management U.S. Environmental Protection Agency

Dear Sir:

We are concerned that the EPA's failure to regulate perchlorate, as well as its unprotective proposed health reference level, will adversely affect the health and development of hundreds of thousands, perhaps millions of American children. In addition, expecting mothers will run the risk of permanently damaging the development of their unborn children. Not only will unborn children be affected, but the elderly population as well. Elderly people with a history of medical conditions will have a difficult time fighting off the effects that perchlorate may have.

Response: See response to comment code 6120.

Commenter Name: Luis Olmedo Vélez
Commenter Organization: omité Cívico del Valle, Inc.
EPA Document ID: EPA-HQ-OW-2008-0692-0652
EPA Comment ID: 19994
EPA Comment Code: 6120

Comment: Imperial Valley undergoes several environmental risks: The air is unclean. Pesticides are used regularly where people may come in contact with it. EPA's inability to contain perchlorate will only add to the already unstable environment in the Imperial Valley.

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-0159
EPA Comment ID: 20015
EPA Comment Code: 6120

Comment: Please don't let more perchlorate into the drinking water.

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #4 - Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-0687
EPA Comment ID: 20016
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

I urge you to set a drinking water standard for perchlorate that will protect pregnant women and babies nationwide. Perchlorate poses a risk for pregnant women, newborns and young children by interfering with thyroid hormone, which is critical for optimal development of the brain and nervous system. Perchlorate is found in drinking water in at least 26 states, and 20-40 million people could be exposed to this chemical.

Several states have set drinking water standards or guidelines for this chemical, but these standards vary widely, so it is critical for the EPA to set a national standard that is based on the best available science and that will protect public health. The EPA's own staff scientists have determined that your decision not to regulate perchlorate places some infants and young children above safe levels of exposure. The EPA's current draft scientific analysis should undergo independent scientific peer review and should be used as the basis for the regulation.

Response: The Agency believes that further review by the National Research Council would unnecessarily delay regulatory decision making for perchlorate. Therefore, EPA is not, at present, planning to request additional NRC review of issues related to perchlorate. Instead, EPA is issued a notice in August of 2009 seeking comments on a broad range of alternative approaches to the interpretation of the scientific data relevant to a regulatory determination for perchlorate in drinking water.

EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #4 - Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-0687
EPA Comment ID: 20018
EPA Comment Code: 6120

Comment: Again, I urge you to reverse your decision and to set a national drinking water standard for perchlorate.

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #5 - Clean Water Fund/Clean Water Action
EPA Document ID: EPA-HQ-OW-2008-0692-0689
EPA Comment ID: 20019
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

* perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought;

* a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Additional Facts

* Perchlorate is a harmful chemical used in rocket fuel, flares, and explosives.

* Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism.

* Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

* EPA agrees that perchlorate has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher.

Response: See response to comment code 6120.

Commenter Name: Pete McHugh
Commenter Organization: Santa Clara County Board of Supervisors
EPA Document ID: EPA-HQ-OW-2008-0692-0681
EPA Comment ID: 20020
EPA Comment Code: 6120

Comment: October 15, 2008

Stephen L. Johnson, Administrator Environmental Protection Agency - Mail Code 2822T 1200 Pennsylvania Avenue, N .W. Washington, D.C. 20460

Re: Docket ID No. EPA-HQ-OW-2008-0692

Dear Mr. Johnson:

The Santa Clara County Board of Supervisors does not agree with the preliminary determination of the Environmental Protection Agency (EPA) to not regulate perchlorate in drinking water at a national level.

Response: See response to comment code 6120.

Commenter Name: Pete McHugh
Commenter Organization: Santa Clara County Board of Supervisors
EPA Document ID: EPA-HQ-OW-2008-0692-0681
EPA Comment ID: 20022
EPA Comment Code: 6120

Comment: In September 2007, the State of California adopted a regulation to establish a maximum contaminant level (MCL) of 6 micrograms per liter for perchlorate in drinking water. However, a national standard is critical to safeguard water supplies throughout the nation and provide a baseline for enforcement by the EPA.

Community health is one of our Board's highest priorities. The protection of our residents through an enforceable drinking water standard for perchlorate is of paramount concern. It is for these reasons, the Santa Clara County Board of Supervisors urges your reconsideration of the need for a national perchlorate standard, and requests the EPA to protect public health by setting a Federal drinking water standard at or below the 6 micrograms per liter established in California.

Sincerely,

Pete McHugh Chair, Board of Supervisors

c: Santa Clara County Board of Supervisors Peter Kutras, Jr., County Executive Jerry Klepner, BKSH and Associate s Santa Clara County Congressional Delegation

COUNTY GOVERNMENT CENTER 70 WEST HEDDING STREET SAN JOSE, CALIFORNIA 95110

TEL: (4O8) 299-5030 FAX: (4O8) 298-6637

Response: See response to comment code 6120.

Commenter Name: P. Grieman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0683
EPA Comment ID: 20024
EPA Comment Code: 6120

Comment: I'm responding as an individual, not an organization, to say that I am appalled that the EPA is refusing to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692).

As is recognized in many countries outside the United States, perchlorate is a harmful chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children. Perchlorate is found in drinking water in 35 states, and according to the EPA's own data, 16 million Americans are at risk of being exposed to this dangerous chemical.

Not regulating this harmful chemical in our drinking water is unacceptable. I urge you to set a standard to protect Americans' health in accordance with the Safe Drinking Water Act.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0688
EPA Comment ID: 20025
EPA Comment Code: 6120

Comment: Please regulate Perchlorate

Response: See response to comment code 6120.

Commenter Name: Brittni
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0690
EPA Comment ID: 20026
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Please still regulate this. Thank you!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0691
EPA Comment ID: 20027
EPA Comment Code: 6120

Comment: reverse this decision.

Response: See response to comment code 6120.

Commenter Name: Karen Parmett

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0693
EPA Comment ID: 20028
EPA Comment Code: 6120

Comment: We must keep rocket fuel and related waste streams out of our public drinking water. Please keep perchlorate out of our drinking water!

yours sincerely,

Karen Parmett 86 Clark St. Belmont MA 02478

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0694
EPA Comment ID: 20029
EPA Comment Code: 6120

Comment: I request that the U.S. Environmental Protection Agency set a regulation for perchlorate in drinking water.

I have been concerned for some time about contamination in our water supply and have researched and now use water purification for my personal home drinking, cooking and bathing water.Perchlorate is one of the contaminants I am concerned about and try to control in our water supply.

I believe that perchlorate contamination is a nationwide problem and poses a general health risk if not regulated and monitored.

A national primary water regulation should include strict levels of perchlorate contamination that would protect the public health.

Please reconsider any decisions that reduce the control of perchlorate in our water supply.

Response: See response to comment code 6120.

Commenter Name: J. Brundage
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0696
EPA Comment ID: 20030
EPA Comment Code: 6120

Comment: Please regulate perchlorate in water. People drink that stuff!

Response: See response to comment code 6120.

Commenter Name: Tricia Telesco
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0697
EPA Comment ID: 20031
EPA Comment Code: 6120

Comment: Perchlorate is a very harmful chemical and once ingested, even in minute amounts, will adversely effect the public's health and safety. I strongly urge the EPA reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Tricia Telesco

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0699
EPA Comment ID: 20032
EPA Comment Code: 6120

Comment: Keep perchlorate out of our drinking water

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0700
EPA Comment ID: 20033
EPA Comment Code: 6120

Comment: Please keep our drinking safe beyond any common sense doubt and regulate perchlorates.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0701
EPA Comment ID: 20034
EPA Comment Code: 6120

Comment: How can the EPA not want to regulate perchlorate? That's a rhetorical question - it's pretty blatantly clear someone is being paid off, again.

Whoever is making these decisions needs to go, so that the EPA can do its job. I for one will support any effort by the EPA employees to oust the corrupt political appointees killing us for money.

Response: See response to comment code 6120.

Commenter Name: L.S. Johnson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0705
EPA Comment ID: 20035
EPA Comment Code: 6120

Comment: Please reverse your preliminary determination on setting a regulation for perchlorate in drinking water. Perchlorate should be regulated. Thank you.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0708
EPA Comment ID: 20036
EPA Comment Code: 6120

Comment: Please regulate perchlorate. It can damage a person's thyroid gland. We have enough medical expenses in this country.

Response: See response to comment code 6120.

Commenter Name: Carol Klingsmith
Commenter Organization: Workout for Wellness
EPA Document ID: EPA-HQ-OW-2008-0692-0709
EPA Comment ID: 20037
EPA Comment Code: 6120

Comment: I feel it is imperative to keep our drinking water clean and safe. Please no Perchlorate in the water.

Response: See response to comment code 6120.

Commenter Name: S. Strohmeyer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0710
EPA Comment ID: 20038
EPA Comment Code: 6120

Comment: Why are you even considering this? Our government should be here to defend us from outside danger, but this is just one more way to hurt our people and our beautiful country. The EPA is supposed to protect us from harm not kill us from the inside.

Response: See response to comment code 6120.

Commenter Name: M. Fiorini

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0712
EPA Comment ID: 20039
EPA Comment Code: 6120

Comment: Perchlorate, at any level, should not be allowed into our drinking water. It is a shame that you have to hold a public response to determine that we should not be drinking perchlorate.

There are many scientific reports that determine perchlorate is unsafe to drink and one does not have to be a rocket scientist to know that rocket fuel is bad for humans and is also bad for all other living creatures. It should not be allowed in our drinking water, regardless of the cost of removal. I know the government has spent more money on less worthwhile causes.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0715
EPA Comment ID: 20040
EPA Comment Code: 6120

Comment: I urge the Environmental Protection agency to do whatever it can to protect the drinking water supply in this country. It remains a highly vulnerable resource, critical to the health and well being of our entire population. Please work to regulate the effects of perchlorate in the water supply.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0717
EPA Comment ID: 20041
EPA Comment Code: 6120

Comment: It is imperative that the EPA regulate perchlorate (an ingredient of rocket fuel) and insist that it be kept out of our drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0721
EPA Comment ID: 20042
EPA Comment Code: 6120

Comment: Perchlorate is Poison. Vote NO on Docket ID: EPA-HQ-OW-2008-0692 Drinking Water: Preliminary Regulatory Determination on Perchlorate Would you want to drink or bathe in this?

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0722
EPA Comment ID: 20043
EPA Comment Code: 6120

Comment: please do not allow perchlorate in the drinking water. If I wanted that in my water I would go out and get it. Try to keep our drinking water as pure as possible. Thank you from someone who drinks a lot of water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0725
EPA Comment ID: 20044
EPA Comment Code: 6120

Comment: Please reconsider your position on percholate, and set standards for it exclusion from drinking water.

Response: See response to comment code 6120.

Commenter Name: J. Rosalia
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0726
EPA Comment ID: 20045
EPA Comment Code: 6120

Comment: Keep PERCHLORATE OUT of the water. It is INSANE to even consider allowing it in.

Response: See response to comment code 6120.

Commenter Name: Molly Lindner
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0732
EPA Comment ID: 20046
EPA Comment Code: 6120

Comment: The drinking water in my locale, North Canton, Ohio, is still not drinkable, in my opinion, without filtering because it has chlorine in it and smells, tastes awful. Please regulate Perchlorate and order local water control officers to purge this chemical from our drinking water.

Thank you.

Dr. Molly Lindner

Response: See response to comment code 6120.

Commenter Name: Luis Olmedo VÃ©lez
Commenter Organization: ComitÃ© CÃvico del Valle, Inc., Center for Health Education, Prevention and Advocacy
EPA Document ID: EPA-HQ-OW-2008-0692-0736
EPA Comment ID: 20047
EPA Comment Code: 6120

Comment: Mr. Burneson, Tell EPA to extend the time comment period to 90 days. Thank you.

Luis Olmedo VÃ©lez Executive Director ComitÃ© CÃvico del Valle, Inc. 699 E Street Brawley, CA 92227 October 24, 2008

Eric Burneson Office of Ground Water and Drinking Water Standards and Risk Management U.S. Environmental Protection Agency

Dear Sir:

We are concerned that the EPAâ€™s failure to regulate perchlorate, as well as its unprotective proposed health reference level, will adversely affect the health and development of hundreds of thousands, perhaps millions of American children. In addition, expecting mothers will run the risk of permanently damaging the development of their unborn children. Not only will unborn children be affected, but the elderly population as well. Elderly people with a history of medical conditions will have a difficult time fighting off the effects that perchlorate may have.

Imperial Valley undergoes several environmental risks: The air is unclean. Pesticides are used regularly where people may come in contact with it. EPAâ€™s inability to contain perchlorate will only add to the already unstable environment in the Imperial Valley.

Response: EPA announced on October 10, 2008, its preliminary regulatory determination that a national primary drinking water regulation for perchlorate would not present "a meaningful opportunity for health risk reduction for persons served by public water systems." In response to requests from several stakeholders, EPA reopened the public comment period for an additional 15 days. Regarding EPA's determination to regulate perchlorate in drinking water, See response to comment code 6120.

Commenter Name: D. Kaufer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0738
EPA Comment ID: 20049
EPA Comment Code: 6120

Comment: Please do not allow percholate in our drinking water

Response: See response to comment code 6120.

Commenter Name: G. Hansen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0741
EPA Comment ID: 20050
EPA Comment Code: 6120

Comment: The U.S. Environmental Protection Agency should reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

There is no reason this country should allow these types of chemicals in our drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0744
EPA Comment ID: 20051
EPA Comment Code: 6120

Comment: Hello, It has come to my attention that the EPA has made a preliminary decision NOT to regulate perchlorate, a rocket fuel, with respect to contamination of drinking water. Considering both the divergent and grave effects to humans upon exposure to this chemical as well as recent studies showing that the chemical is dangerous at lower levels than previous thought, it is outrageous that the EPA would make such a poor decision. Please reconsider in favor of regulating perchlorate for the sake of our health and especially the health of our babies and developing fetuses.

Response: See response to comment code 6120.

Commenter Name: K. Minissale
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0746
EPA Comment ID: 20052
EPA Comment Code: 6120

Comment: Even though percholate is only found to affect a very small percentage of the population (by geographical location), a national health standard should be set in light of the fact that all people, even minority groups, deserve protection of their basic health condidtions and that having a national standard in place can only benefit others in the future should greater affected areas be discovered.

Response: See response to comment code 6120.

Commenter Name: R. Cubberly
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0747
EPA Comment ID: 20053

EPA Comment Code: 6120

Comment: Keep Perchlorate out of our drinking water!! Please reverse your decision!

Response: See response to comment code 6120.

Commenter Name: V. Hollen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0748
EPA Comment ID: 20054
EPA Comment Code: 6120

Comment: I urge the EPA to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. It has several potential health consequences: impaired thyroid gland, child developmental impairment including mental retardation, deficits in motor skills... Please be the clarion to declare the the US government is going to protect its citizens from contaminated water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0749
EPA Comment ID: 20055
EPA Comment Code: 6120

Comment: Water is our most precious resource. I think the EPA needs to rethink its decision and start better protecting our water supply by regulating the amount of percholate in our drinking water. We should all be comfortable drinking from the tap in our homes, not constantly worrying about what contaminate has now found its way into our wells and water supplies. No one trusts the water as can be seen by the rise in purchasing of bottled water. It's your job to keep our water safe. Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought. A national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Response: See response to comment code 6120.

Commenter Name: J. Traweek
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0752
EPA Comment ID: 20057
EPA Comment Code: 6120

Comment: We are very concerned that the EPA will not be exercising its regulatory authority and the statutory purpose for its existence if the EPA does not take the needed steps to safeguard America's water quality by regulating the contamination of our water with perchlorate. Thank you

Response: See response to comment code 6120.

Commenter Name: K. McDonald
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0754
EPA Comment ID: 20058
EPA Comment Code: 6120

Comment: I strongly urge this agency to reconsider it's decision to allow unlimited polution of our drinking water supplies with Perchlorate. Remember you and your family is drinking this water too.

Response: See response to comment code 6120.

Commenter Name: Raymon A. Baldoni
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0755
EPA Comment ID: 20059
EPA Comment Code: 6120

Comment: I have survery several dozen people in my neighberhood and 100% are against the EPA's tentative decision not to regulate perchlorate in drinking water. This decision is not in the best interests of the public and appears to be complete fiscally motivated. Our health and the health of our children is not negotiable and should not be relaxed to "reasonable care" standards. The EPA needs to be aggressive in setting all air and water standards to a best practice standard and deamnd funding to enable the agressive enforcement of these standards.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0757
EPA Comment ID: 20060
EPA Comment Code: 6120

Comment: I URGE YOU TO RECONSIDER YOUR DECISION NOT TO REGULATE PERCHLORATE IN DRINKING WATER. I AM CONCERNED ABOUT THE HEALTH IMPACTS, PARTICULARLY ON INFANTS AND CHILDREN. PLEASE TAKE ACTION TO PROTECT OUR WATERS AND THE PUBLIC HEALTH. THANK YOU.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0761
EPA Comment ID: 20061
EPA Comment Code: 6120

Comment: ALL chemicals that can get into our drinking water should be monitored and regulated. I am curious as to why you would NOT monitor and regulate such things.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0762
EPA Comment ID: 20062
EPA Comment Code: 6120

Comment: Please continue to regulate Perchlorate and all the chemicals which may be harmful in our drinking water. I urge you to reverse your preliminary decision on this.

Response: Perchlorate is not regulated in drinking water. See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0767
EPA Comment ID: 20063
EPA Comment Code: 6120

Comment: You must work to regulate rocket fuel in our drinking water. This is not optional, we need all the safeguards in place to make sure our safe drinking water, which is becoming ever more precious and scarce, remains so. It could be improved in so many ways, but certainly this is an easy one to regulate. Thank you!

Response: See response to comment code 6120.

Commenter Name: G. E. Andrews
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0769
EPA Comment ID: 20064
EPA Comment Code: 6120

Comment: Perchlorate in our drinking water is unacceptable. We need your leadership to make the right decision immediately to protect human health.

Response: See response to comment code 6120.

Commenter Name: Roger N. Carlsten
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0770
EPA Comment ID: 20065
EPA Comment Code: 6120

Comment: I strongly urged the EPA to take any action necessary to eliminate percholates from our national drinking water. Not just because I already suffer from hypothyroidism, but how it adversely affects all citizens, especially developing fetuses and young children.

Sincerely,

Roger N. Carlsten, D.D.S.

Response: See response to comment code 6120.

Commenter Name: Anita Burns
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0771
EPA Comment ID: 20066
EPA Comment Code: 6120

Comment: What is it that makes you think I want to have water with this chemical in it! There should be criminal action taken to those that disposed this chemical into the water system & they should have to pay to clean up this mess!. Our health is more important than letting this chemical stay in the water. I am strongly opposed to having this chemical in the water!!!!! Perchlorate is a harmful chemical used in rocket fuel, flares, and explosives. Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills. Anita Burns ...bosburns@wowway.com

Response: See response to comment code 6120.

Commenter Name: H. Passas
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0772
EPA Comment ID: 20067
EPA Comment Code: 6120

Comment: I wish to urge the EPA to reconsider the preliminary decision not to regulate perchlorate in drinking water. This is a harmful substance that can damage the thyroid, thus affecting growth, development and metabolism at minute exposure levels, especially in babies in small children. Perchlorate has already been found in the drinking water consumed by millions of US citizens. I think it is unconscionable for the government agency that has the obligation to protect the environment which sustains us all to fail in its task of regulating dangerous substances!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0774
EPA Comment ID: 20068
EPA Comment Code: 6120

Comment: Please protect our health and well-being through the regulation of perchlorate in drinking water. It is a lethal contaminant not for consumption. Your responsibility is to protect the environment, not damage it and its inhabitants.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0776
EPA Comment ID: 20069
EPA Comment Code: 6120

Comment: It is the responsibility of the EPA to regulate perchlorate in drinking water. I urge you, the U.S. Environmental Protection Agency, to reverse your preliminary determination on setting a regulation for perchlorate in drinking water. Here are a few facts on perchlorate:

* perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought;

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0776
EPA Comment ID: 20071
EPA Comment Code: 6120

Comment: I know perchlorate is found in drinking water and drinking water source areas because I worked on the assessment and remediation of contaminated and potentially contaminated properties in New England that had perchlorate. The people of the US depend on you to protect their drinking water. You must take the lead in establishing and enforcing a drinking water perchlorate regulation.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0778
EPA Comment ID: 20076
EPA Comment Code: 6120

Comment: Keep perchlorate out of our drinking water supply.

Response: See response to comment code 6120.

Commenter Name: Richard
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0780
EPA Comment ID: 20077
EPA Comment Code: 6120

Comment: The regulation or perchlorates in drinking water should be established as soon as possible. this harmful chemical poses a threat to humans and should be dealt with accordingly..

thank you. Richard

Response: See response to comment code 6120.

Commenter Name: Linda D. Hrushanyk
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0782
EPA Comment ID: 20078
EPA Comment Code: 6120

Comment: After reading some of the facts on perchlorate and the potential health problems the chemical can cause, don't you think regulating the amount of perchlorate would prevent some health problems?

linda d. hrushanyk

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0783
EPA Comment ID: 20079
EPA Comment Code: 6120

Comment: Keep ariplane fuel out of our water, perchlorate does not belong in our drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0784
EPA Comment ID: 20080
EPA Comment Code: 6120

Comment: Please do not lower the standards for clean water. As a member of the public I would prefer my drinking water to be free of rocket fuel. Thank you

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0785
EPA Comment ID: 20081
EPA Comment Code: 6120

Comment: Please regulate perchlorate in drinking water. I am sure the science exists to filter it so we should use it.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0787
EPA Comment ID: 20082
EPA Comment Code: 6120

Comment: Regulate Perchlorate in our drinking water!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0788
EPA Comment ID: 20083
EPA Comment Code: 6120

Comment: Perchlorate has leaked into our water supplies everywhere, though particularly in the western and southwestern United States. It has turned up in our lettuce!

Ingredients of rocket fuel do not belong in our water. And if our tap water isn't clean, we're paving the way for the privatization of water, which means only the rich people will have water and the rest of us will have to fight each other for it.

Keep the water clean and get perchlorate out of our water. This one's a no- brainer.

Response: See response to comment code 6120.

Commenter Name: Mary Green
Commenter Organization: Eleventh Street Family Health Service Center
EPA Document ID: EPA-HQ-OW-2008-0692-0789
EPA Comment ID: 20084
EPA Comment Code: 6120

Comment: q-OW-2008-0068To: Councilman Curtis J. Jones 4th District Room 404 Phila. PA 19107

In regard to contamination of our water and the water regulations please support identified as Water regulations Docket ID No. EPA-HQ-OW-2008-0068. The EPA will make final determinations on this health advisory for percholorate of contamination into our water supply and the regulation of it. Please consider looking inot this. thank you. Mary Green MSN, RN . Eleventh Street Family Health Service Center 850 11th Street Phila. PA 19123 Attachments [see PDF of Docket ID EPA-HQ-OW-2008-0692-0789]

EPA-HQ-OW-2008-0692-0789.1 Comment attachment submitted by Curtis J. Jones, Philadelphia City Council

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0790
EPA Comment ID: 20085
EPA Comment Code: 6120

Comment: We don't need rocket fuel in our drinking water. If you are planning to join Bush and company on a remote island after looting the treasury, you might think that you're safe from it, but you're not. And if you're an alcoholic that denies being in a water-based environment, clear your thinking for a moment and figure out that everything that you eat has water in it. Tap water, for the most part. No, even living on bottled water won't get you away from perchlorate, as most plastic bottles have perchlorate in them. It won't do anyone good to relax rules that are there to protect all of us. Just don't change the rules!

Response: See response to comment code 6120.

Commenter Name: L. Thorp
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0791
EPA Comment ID: 20086
EPA Comment Code: 6120

Comment: Please regulate Perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0792
EPA Comment ID: 20087
EPA Comment Code: 6120

Comment: Please make sure that the standard for drinking water in the USA is one that does not allow for perchlorate. Thank you

Response: See response to comment code 6120.

Commenter Name: C. Smith
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0798
EPA Comment ID: 20088
EPA Comment Code: 6120

Comment: There is no reason or excuse not to regulate Perchlorate that affects our drinking water.

Response: See response to comment code 6120.

Commenter Name: Pamela Love Koepf
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0801
EPA Comment ID: 20089
EPA Comment Code: 6120

Comment: Please do not allow our water to be unregulated for Perchlorate. We need any and all help to monitor all innappropriate invasives in our drinking and open water supply. If you guys don't do it, who will? Please reverse this important decision for the sake of all of us!

Pamela Love Koepf Bellevue, WA

Response: See response to comment code 6120.

Commenter Name: C. P. Gabelman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0804
EPA Comment ID: 20090
EPA Comment Code: 6120

Comment: I believe the mandate of the EPA is to protect our nation's citizens - not our nation's corporations. So please, get out of political mode and get back into protection mode and start carrying out your mandate to provide a safe environment for me, my children, my grandchildren and beyond. Perchlorate has no business being in our drinking water supply. Please quit waiting for a crisis to develop before you have the backbone to do your job.

Response: See response to comment code 6120.

Commenter Name: C. Springer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0805
EPA Comment ID: 20091
EPA Comment Code: 6120

Comment: We don't know how to do it. We trust that drinking water and water that is home to aquatic animals will be protected from rocket fuel. thank you for your work.

Response: See response to comment code 6120.

Commenter Name: Tana Moore
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0807
EPA Comment ID: 20092
EPA Comment Code: 6120

Comment: To the U.S. Environmental Protection Agency - please reverse your preliminary determination on regulating perchlorate in drinking water. This is a substance known to cause

thyroid damage. The public and wildlife need protection from such substances in our water. Thank you.

Tana Moore 21472 Wallace Drive Southfield MI 48075

Response: Please See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0811
EPA Comment ID: 20093
EPA Comment Code: 6120

Comment: No Perchlorate in the drinking water, please!

Response: See response to comment code 6120.

Commenter Name: R. Stevenson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0812
EPA Comment ID: 20094
EPA Comment Code: 6120

Comment: Please don't let our drinking water be contaminated by Perchlorate. Clean water is becoming more and more rare and you are risking the future by allowing this chemical to enter our lakes and streams. Please ask yourself if you would be okay with letting your children or grand children consume water or fish in a stream with Perchlorate in it. Thank you for your consideration in this matter.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0813
EPA Comment ID: 20095
EPA Comment Code: 6120

Comment: Please regulate perchlorate. It's meant for rockets not people.

Response: See response to comment code 6120.

Commenter Name: D. and A. M. Wahl Edwards
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0816
EPA Comment ID: 20096
EPA Comment Code: 6120

Comment: Keep perchlorate out of our water supply via regulation. Please protect our future by protecting the fetuses carried in our mothers' wombs.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0819
EPA Comment ID: 20097
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. We need to maintain good quality drinking water and regulate poisons such as this. Please continue to regulate this poison for the welfare of US citizens.

Response: Perchlorate is not regulated in drinking water. See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0822
EPA Comment ID: 20098
EPA Comment Code: 6120

Comment: Please regulate amounts of perchlorate in America's drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0823
EPA Comment ID: 20099
EPA Comment Code: 6120

Comment: There is no reason to believe perchlorate is harmless.Since there is more evidence it is harmful to our health does it not make sense for the EPA to be proactive in regulating it rather than risking our health? Scientific studies that are without influence of any industry need to become the standard so that your agency can function with some degree of integrity.The US was once a leader in environmental issues and we need to get back to that level.

Response: See response to comment code 6120.

Commenter Name: Adam Nation
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0825
EPA Comment ID: 20100
EPA Comment Code: 6120

Comment: Dear Sir/Madam:

It has come to my attention that the EPA, under the leadership of President Bush, has refused to regulate the presence of perchlorate in American drinking water. I urge the Agency to reconsider this decision. Perchlorate is a chemical that has been linked to numerous deleterious health effects in humans (and other animals)-- including serious changes in the thyroid gland, and a potential impact on cognition and normal fetal development.

For these reasons, I urge the EPA to regulate perchlorate very strictly.

Cordially,

Adam Nation Pittsburgh, PA

Response: See response to comment code 6120.

Commenter Name: Dina C. Greenway
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0827
EPA Comment ID: 20101
EPA Comment Code: 6120

Comment: As we look hopefully toward a new attitude about our environment, we look to the EPA to set sound policy. Father Bush is waving goodbye. And the American people look forward to greater ease as you work to protect our health and give a second chance to an environment now on life support.

Let your first act be to reverse to research and regulate for PERCHLORATE in our drinking water.

I thank you, and do a landslide majority of your constituents.

:) :) :) :) dina

Response: See response to comment code 6120.

Commenter Name: D. Toolanen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0828
EPA Comment ID: 20102
EPA Comment Code: 6120

Comment: Please forbid any perchlorates to enter any water systems. The costs and suffering of it are carried by the innocent victims, people, animals, insects, birds, whose physiology will be negatively impacted by these unnatural and toxic chemicals.

Response: See response to comment code 6120.

Commenter Name: Nikki Black

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0829
EPA Comment ID: 20103
EPA Comment Code: 6120

Comment: Every day I seem to hear about friends and loved ones dealing with often fatal illnesses or struggling with conditions that come from our polluted environment. It is extremely disturbing to read that perchlorate, found in studies to impair the thyroid gland as well as the development of infants, has been found in our drinking water and the epa is not requiring that it be eliminated. How can we not protect something so essential as drinking water and make it as pure as possible? I firmly believe the epa should do whatever is possible to eliminate the existence of perchlorate in our drinking water.

Nikki black michigan

Response: See response to comment code 6120.

Commenter Name: L.W. DeLap
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0830
EPA Comment ID: 20104
EPA Comment Code: 6120

Comment: The evidence is clear that perchlorate is toxic. Contamination is widespread. Federal regulation of the level of perchlorate in public drinking water is needed to protect the US population.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0831
EPA Comment ID: 20105
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to rise above the political machinations surrounding this issue and reverse its preliminary determination on setting a regulation for perchlorate in drinking water. It is important that the American public can rely on the EPA making decisions based solely on scientifically determined health risks rather than on potential risks to special interest groups.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0833
EPA Comment ID: 20106
EPA Comment Code: 6120

Comment: We want clean safe drinking water shouldn't that be obvious, don't you?

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0838
EPA Comment ID: 20107
EPA Comment Code: 6120

Comment: Please control percholorate in drinking water- humans are part of the environment and we too need protection. We already have had thyroid cancer in our household, and since this chemical attacks the thyroid, we do not want to again deal with this issue.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0841
EPA Comment ID: 20109
EPA Comment Code: 6120

Comment: Any and all contaniments must be regulated in our public drinking water, no matter how small the threat.

Response: See response to comment code 6120.

Commenter Name: Anne Hall
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0847
EPA Comment ID: 20110
EPA Comment Code: 6120

Comment: Keep perchlorate out of our drinking water! Its a dangerous chemical and all Americans deserve to at least trust that the major substance that we all need to stay alive is safe to drink! It is ridiculous to even call yourselves the "Environmental Protection" Agency if this is the kind of contamination you would consider allowing.

I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Sincerely, Anne Hall Austin, TX

Response: See response to comment code 6120.

Commenter Name: Marjorie Curtiss
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0850
EPA Comment ID: 20111

EPA Comment Code: 6120

Comment: To Whom This May Concern;

In my opinion this is "everyones" concern!

Please do not relax any regulations on drinking water safety, ever. Do we really have to keep bringing topics like this to the attention of the Federal Government? This is a "no brainer" fella's...YOU are the EPA! Sincerely, Marjorie Curtiss

Response: EPA is not "relaxing any regulations on drinking water safety," rather EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: S. Spencer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0852
EPA Comment ID: 20112
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. We must be able to provide clean, safe water to Americans and perchlorate contamination is a serious issue. Please take the responsible action and reverse this decision.

Response: See response to comment code 6120.

Commenter Name: Susan Luberto
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0853
EPA Comment ID: 20113
EPA Comment Code: 6120

Comment: I feel we have to protect our drinking water from any problems that could harm us now and later in life, please follow up and check on the Perchorate that is in the water to make sure it does not stay there.

Thank you.Susan Luberto

Response: See response to comment code 6120.

Commenter Name: L. Thorp
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0858
EPA Comment ID: 20114
EPA Comment Code: 6120

Comment: Please no perchlorate in the water. What will be allowed next?

Response: See response to comment code 6120.

Commenter Name: Kathleen Abke
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0861
EPA Comment ID: 20115
EPA Comment Code: 6120

Comment: I believe it is a mistake to not regulate perchlorate in our drinking water. Please reverse your decision.

Kathleen Abke Grosse Pointe Woods, MI

Response: See response to comment code 6120.

Commenter Name: T. Harris
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0862
EPA Comment ID: 20116
EPA Comment Code: 6120

Comment: I urge the EPA to reverse its decision not to regulate perchlorate in drinking water supplies. This is a nasty chemical that I certainly do not want in my water, regardless of the impacts such legislation might have on industry. People's health should always come before any economic implications.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0864
EPA Comment ID: 20117
EPA Comment Code: 6120

Comment: Nobody wants rocket fuel in their drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0867
EPA Comment ID: 20118
EPA Comment Code: 6120

Comment: This should be an easy decision; do you want your grandchildren drinking water tainted with perchlorate? Do you think anyone in this country wants that? I can only think that the makers of perchlorate would not object to such a contamination but in someone else's water, not their own.

Since you should be concerned with the public's health it is confusing that you would even consider such a thing.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0871
EPA Comment ID: 20119
EPA Comment Code: 6120

Comment: please do not allow perchlorate in drinking water

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0873
EPA Comment ID: 20120
EPA Comment Code: 6120

Comment: I urge the U. S. Environmental Protection Agency to reverse its peliminary detemintion on setting a regulation for perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name:
Commenter Organization: Bethlehem Area School District
EPA Document ID: EPA-HQ-OW-2008-0692-0874
EPA Comment ID: 20121
EPA Comment Code: 6120

Comment: Why is this even an issue? If perchlorate is used in jet fuel...it does NOT belong in our drinking water. Let's just clean up our act regarding water instead of adding more chemicals to it to kill whatever is in there already! Water should not be an issue as far as priority. Please get it cleaned up the correct way. (Floride is next...it was used to kill rats...and it's in many water systems, ugh!!!)

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0875
EPA Comment ID: 20122
EPA Comment Code: 6120

Comment: To Whom it May Concern,

Please reverse your preliminary determination in regard to regulating perchlorate in drinking water. Even small amounts can affect our public health and that of our children. Please take your role as a protector of our environment seriously.

LL Franklin, MA

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0876
EPA Comment ID: 20123
EPA Comment Code: 6120

Comment: I am not from a government agency or an official representative. But what I do represent is my family and most importantly, my children. Our drinking water needs to be safe for the American people and considering to not regulate possible contaminants such as perchlorate is very detrimental to all of our health and well being. Please reconsider this docket and do not pass it. We need our drinking water regulated.

Thank You.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0877
EPA Comment ID: 20124
EPA Comment Code: 6120

Comment: No rocket fuel in our drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0879
EPA Comment ID: 20125
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: C. H. Lynt
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0880

EPA Comment ID: 20126
EPA Comment Code: 6120

Comment: As an Engineer with an advanced degree, and an attorney, I am hereby urging the EPA (U.S. Environmental Protection Agency) to reverse its preliminary decision not to regulate perchlorate in drinking water.

My reasons include the following:

It is well established that perchlorate contamination is a nationwide problem. Perchlorate contamination has been shown (citations omitted) to have health effects at lower levels than previously understood.

A nationwide standard for primary drinking water regulation would provide an important and meaningful opportunity to protect the public health.

Perchlorate is a harmful chemical used, for example, in rocket fuel, flares, and explosives.

In small amounts, perchlorate can impair the thyroid gland, which regulates growth, development and metabolism.

It is well known that developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

The EPA has evidence that perchlorate has been found in at least 395 sites in 37 states, including 153 public water systems serving over 20 million people. Many reliable estimates suggest an even wider contamination.

This is an important public health issue that needs to be addressed in a responsible manner.

Response: Please see the response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0881
EPA Comment ID: 20127
EPA Comment Code: 6120

Comment: No Perchlorate in our drinking water. If there aren't already enough worries about what is already allowed in our drinking water, why this too?

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0882
EPA Comment ID: 20128
EPA Comment Code: 6120

Comment: Please reverse your decision. We do NOT want perchlorate in our drinking water! It needs to be regulated.

Response: See response to comment code 6120.

Commenter Name: Elizabeth A. Carapico
Commenter Organization: Arrowroot Natural Foods, LLP
EPA Document ID: EPA-HQ-OW-2008-0692-0888
EPA Comment ID: 20129
EPA Comment Code: 6120

Comment: To the EPA Personnel:

Your very name indicates your obligation to protect the environment and the vegetation and animal life (including people) dependent on that environment.

Knowingly allowing a dangerous contaminant into the water supply is paramount to putting it there with your own hand; and thus the dangerous ramnifications are on your shoulders personally.

Anything that has a negative effect should be regulated to the nth degree.

Perchlorate falls into this catagory.

I urge you to keep perchlorate out of our drinking water.

Thank you.

Response: See response to comment code 6120.

Commenter Name: Shanoah LaPatka
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0894
EPA Comment ID: 20130
EPA Comment Code: 6120

Comment: Explain to me why perchlorate is not being regulated. It should be banned. Anything that is not naturally found in water should not be added to it. With all the facts how can you even be questioning it. Because of the added expense to remove it or not put it there at all? We can't live without clean water! This is a no brainer!

Thank you, Shanoah LaPatka

Response: See response to comment code 6120.

Commenter Name: Elise Roman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0895

EPA Comment ID: 20131
EPA Comment Code: 6120

Comment: It is important to do everything possible to provide to keep our drinking water clear of Perchlorate. It is outrageous to think that any levels would be acceptable for consumption by anyone, let alone the sick, elderly, young and those with compromised immune systems.

This is a nationwide problem that needs to be addressed. It is more costly to deal with the adverse affects of Perchlorate in our drinking water than to deal with health effects on our general populations.

Please regulate and ban this substance from our drinking water.

Elise Roman

Response: See response to comment code 6120.

Commenter Name: P. Nardizzi
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0899
EPA Comment ID: 20132
EPA Comment Code: 6120

Comment: Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Committee for people who don;t want to die. Bring back the American Indian

Response: See response to comment code 6120. The American Indian is outside the scope of this notice.

Commenter Name: James Gambucci
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0903
EPA Comment ID: 20133
EPA Comment Code: 6120

Comment: Hello.

Please keep Perchlorate out of our water!!

Thank you.

-James Gambucci

Response: See response to comment code 6120.

Commenter Name: John Porzondek
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-0904
EPA Comment ID: 20134
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Nothing should be in water except WATER.

Please stop it for our children's and future's sake.

Thank you, John Porzondek 790 Lake Street Saugatuck, MI 49453-9435

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0910
EPA Comment ID: 20135
EPA Comment Code: 6120

Comment: Please keep poison out of the water!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0913
EPA Comment ID: 20136
EPA Comment Code: 6120

Comment: a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0914
EPA Comment ID: 20137
EPA Comment Code: 6120

Comment: I support regulations and legislation that keeps perchlorate out of our drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-0915
EPA Comment ID: 20138
EPA Comment Code: 6120

Comment: No perchlorate in our water!!! None!

Response: See response to comment code 6120.

Commenter Name: Jeffrey Ramsey
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0920
EPA Comment ID: 20139
EPA Comment Code: 6120

Comment: I urge the US EPA to reconsider its position on the regulation of perchchlorate in drinking water. This is a nationwide problem. Perchchlorate-contaminated drinking water has been found to to have negative health impacts at lower levels than previously recorded, particularly affecting the thyroid gland of developing fetuses, infants and children. Our children deserve protection through regulation of this hazardous contaminant.

Please reverse your decision concerning perchchlorate regulation.

Kind regards, Jeffrey Ramsey 3315 Heidelberg Drive Boulder, CO 80305

Response: See response to comment code 6120.

Commenter Name: G. MacCallum
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0923
EPA Comment ID: 20140
EPA Comment Code: 6120

Comment: You are insane to consider this. Fresh, clean water, so deeply necessary to all life, must be protected. Consideration of "acceptable" levels of any one chemical cannot exclude conscious study of how the myriad of other toxins and pharmaceuticals flowing into our environment in combination impact human life.

Response: See response to comment code 6120.

Commenter Name: Alex Milbank
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0924
EPA Comment ID: 20141
EPA Comment Code: 6120

Comment: Perchlorate is dangerous and should not be allowed in drinking water supplies. Please reverse your decision and protect humans and the environment. Thank you for your consideration. Alex Milbank

Response: See response to comment code 6120.

Commenter Name: Sarah Smith
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0925
EPA Comment ID: 20142
EPA Comment Code: 6120

Comment: I don't want rocket fuel in my drinking water. Please reverse your decision and regulate water for perchlorate. It is very harmful to human health and should not be in our drinking water.

Thank you,

Sarah Smith citizen Belmont, MA

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0929
EPA Comment ID: 20143
EPA Comment Code: 6120

Comment: If the government is aware of the presence of a potentially harmful contaminant in drinking water, it is their obligation to monitor it, study the health effects and fully understand the threat to the best of its ability. To do otherwise, such as ignoring it, is negligent.

Please regulate perchlorate.

Response: See response to comment code 6120.

Commenter Name: M. Doyle
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0932
EPA Comment ID: 20144
EPA Comment Code: 6120

Comment: I do not understand why the EPA would allow anything in our drinking water that is not supposed to be there even if there is not â€˜â€˜a meaningful opportunity for health risk reduction for persons served by public water systems.â€™â€™ Please regulate the water so that we are not drinking Perchlorate!

Response: See response to comment code 6120.

Commenter Name: W. Petry
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0933

EPA Comment ID: 20145
EPA Comment Code: 6120

Comment: Plaese continue to regulate perchlorates in our drinking water.

Response: EPA does not currently regulate perchlorate in drinking water; however, EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: E. Ralph
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0934
EPA Comment ID: 20146
EPA Comment Code: 6120

Comment: We should not have perchlorate in our drinking water. Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought. The last months of a presidency is not the time to be rushing through controversial regulation.

Response: See response to comment code 6120.

Commenter Name: Roberta Masters-Cullen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0936
EPA Comment ID: 20147
EPA Comment Code: 6120

Comment: Dear Sir/Madam,

I strongly urge you to remember the environmental PROTECTION part of your agency's philosophy and ask you to please regulate perchlorate in our drinking water. Your department was founded to protect us - please don't let an ingredient that's used in rocket fuel go unregulated in our drinking water.

Roberta Masters-Cullen Alexandria, Virginia

Response: See response to comment code 6120.

Commenter Name: D. Fahrmann
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0938
EPA Comment ID: 20149
EPA Comment Code: 6120

Comment: As with all chemicals in the water...you know it will affect animals and humans in a negative way. You don't need to spend millions to figure it out -just attack the problem in any way you can to reduce the levels of the chemical.

At a minimum, the EPA needs to regulate Perchlorate.

Response: See response to comment code 6120.

Commenter Name: W. Calvert
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0941
EPA Comment ID: 20150
EPA Comment Code: 6120

Comment: Dear EPA,

Please control the amount of perchlorate in our drinking water. This substance is harmful to human health. Not only is it your duty to do this, it is the morally correct thing to do.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0942
EPA Comment ID: 20151
EPA Comment Code: 6120

Comment: Please keep drinking water clean for everyone

Response: This is not a comment, no response is needed.

Commenter Name: Elizabeth Saunders
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0943
EPA Comment ID: 20152
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to regulate perchlorate in drinking water. The preliminary determination to refrain from setting such a regulation is irresponsible.

Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought. As someone with an impaired thyroid gland I do not like considering the possibility that my drinking water might at any time contain a chemical known to cause thyroid damage. I hate to think (not that I will ever know) that this might be the cause, or that drinking contaminated water would worsen my health.

To ignore this problem and avoid setting a standard for perchlorate in drinking water is inappropriate. We citizens count on our government agencies to protect our water and our health and this is one example of where that is necessary.

Please reverse the determination.

Sincerely, Elizabeth Saunders Dorchester, MA 02122

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0945
EPA Comment ID: 20153
EPA Comment Code: 6120

Comment: I am writing to urge the EPA to please regulate perchlorate in our drinking water. I type medical reports for an Oncology Center. Cancer rates are skyrocketing in this country. We don't need another contaminant to make the situation worse.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0948
EPA Comment ID: 20154
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: G. Breese
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0949
EPA Comment ID: 20155
EPA Comment Code: 6120

Comment: It is vitally important to the health and safety of all Americans, particularly children and developing fetuses, that the EPA reverse its finding and regulate perchlorate to keep it out of our drinking water! Such chemicals in our daily drinking water can do more long and short term damage than any terrorist could ever hope to do. Please reverse your decisions and keep Americans strong and healthy -- don't contribute to weakening our country just to save a few dollars. Thank you.

Response: See response to comment code 6120.

Commenter Name: M. Roberts
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0951
EPA Comment ID: 20156
EPA Comment Code: 6120

Comment: Please DO regulate the perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0952
EPA Comment ID: 20157
EPA Comment Code: 6120

Comment: Perchlorate needs to be regulated.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0954
EPA Comment ID: 20158
EPA Comment Code: 6120

Comment: We need to keep our water clean! I hope you will reverse this decision and regulate this chemical.

Response: See response to comment code 6120.

Commenter Name: Jerise Fogel
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0957
EPA Comment ID: 20159
EPA Comment Code: 6120

Comment: What is the EPA for, if not to regulate items such as this? I have no idea why adding Perchlorate to the list of regulated chemicals that should not be added to drinking water would be a sticking point for my Environmental Protection Agency, unless some large producer(s) of Perchlorate who habitually let them leach into our drinking water is/are paying someone off.

EPA, please do your job. Regulate Perchlorate!

Sincerely,

Jerise Fogel

Response: See response to comment code 6120.

Commenter Name: Angela Christman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0960
EPA Comment ID: 20160
EPA Comment Code: 6120

Comment: Reverse this decision!! This is a bad decision which is bad for the environment and for our health! Reverse it now!

Angela Christman Catonsville, MD 21228

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0964
EPA Comment ID: 20161
EPA Comment Code: 6120

Comment: How can anyone imagine any amount of perchlorate is tolerable or safe in drinking water? It must also be banned in water for irrigation of crops and for animals. This chemical is toxic, toxic, toxic!!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0965
EPA Comment ID: 20162
EPA Comment Code: 6120

Comment: Reverse your finding and regulate perchlorate in drinking water!!!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0967
EPA Comment ID: 20163
EPA Comment Code: 6120

Comment: Please ban Perchlorate from drinking water!! Nobody wants to drink that, just so the companies who produced it have an easier way of getting rid of it!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0970
EPA Comment ID: 20164
EPA Comment Code: 6120

Comment: I URGE THE U.S. ENVIRONMENTAL PROTECTION AGENCY TO REVERSE ITS PRELIMINARY DETERMINATION ON SETTING A REGULATION FOR PERCHLORATE IN DRINKING WATER.

Response: See response to comment code 6120.

Commenter Name: Philip Katz
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0971
EPA Comment ID: 20165
EPA Comment Code: 6120

Comment: I am a strong supporter of regulations maintaining clean air and water. Therefore I ask that you regulate the amount of percholate in our water supply. I ask that you make the level as scientifically possible.

Thank you,

Philip Katz Citizen 37 Kensington Ave. West Newton, Ma 02465 philkatz@rcn.com

Response: See response to comment code 6120.

Commenter Name: Kristin Flora
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0973
EPA Comment ID: 20166
EPA Comment Code: 6120

Comment: Please regulate Percholarate in our water. We know that certain levels of this chemical have been found to be harmful. Why would you want to intentionally ignore the levels of this harmful chemical in the water that we drink? Please reconsider your decision concerning the regulation of this harmful checmical.

Kristin Flora South Riding, VA

Response: See response to comment code 6120.

Commenter Name: S. Picciuca
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0976
EPA Comment ID: 20167
EPA Comment Code: 6120

Comment: Water uncontaminated is the right of all living beings on this planet.Our security begins with safe water and nothing supercedes it.Please do your duty.

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0977
EPA Comment ID: 20168
EPA Comment Code: 6120

Comment: Why on earth would you allow Perchlorate in my drinking water? This is not acceptable. Please fix this!

Response: See response to comment code 6120.

Commenter Name: J. V. Blargan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0983
EPA Comment ID: 20169
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. In California, perchlorate contamination in the groundwater has literally poisoned wells, and now it's okay, somehow?

Studies are already showing health impacts at lower levels than previously imagined and threatens of water supply. We need a national primary drinking water regulation to protect public health.

Bisphenol-A and Perchlorate are in a class of endocrine disrupters that impair the thyroid gland, which controls growth, metabolism, and development, especially in fetuses, infants and children.

EPA agrees that perchlorate has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0984
EPA Comment ID: 20170
EPA Comment Code: 6120

Comment: I can't believe there would even be a question as to whether or not to regulate the amount of perchlorate in water. What could possibly be a plausible reason? For the sake of children alone, this should be a no-brainer. The fact that there is even a question is frankly disgusting to me. Our government at work looking out for our best interest, obviously. I hope no one at the EPA has a pregnant wife or children gulping down the contaminated water. Do what's right, no matter what the cost!! We are talking about people's health here!

Response: See response to comment code 6120.

Commenter Name: B. Steinmetz

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0991
EPA Comment ID: 20171
EPA Comment Code: 6120

Comment: Please. I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Nothing is more important than public heath.

Response: See response to comment code 6120.

Commenter Name: Richard Lee
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0994
EPA Comment ID: 20172
EPA Comment Code: 6120

Comment: I can't believe that anyone actually has to write to express their concern against not regulation a poison in our drinking water. What is going on here? Please reverse this reckless and devastating decision before more people are poisoned.

Thank you for your consideration. Richard Lee, Berkley, MI

Response: See response to comment code 6120.

Commenter Name: D. Edwards
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0995
EPA Comment ID: 20173
EPA Comment Code: 6120

Comment: EPA must regulate Perchlorate in drinking water! It is too dangerous for public health.

Response: See response to comment code 6120.

Commenter Name: T. Coutinho
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0998
EPA Comment ID: 20174
EPA Comment Code: 6120

Comment: Our water must be protected.....

Response: This is not a comment, a response is not necessary.

Commenter Name: L. C.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1000

EPA Comment ID: 20175
EPA Comment Code: 6120

Comment: I urge the EPA to reconsider their decision not to regulate perchlorates in the drinking water.

Perchlorates can have a negative effect on the thyroid gland which impacts the development and growth of born and unborn children. We need to protect our drinking water and our health.

Thank you. L.C.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1004
EPA Comment ID: 20176
EPA Comment Code: 6120

Comment: Please, NO rocket fuel allowed in the water!!!!!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1005
EPA Comment ID: 20177
EPA Comment Code: 6120

Comment: As a citizen and a volunteer leader for the Boy Scouts of America, this just doesn't sound right to me. I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Water is the essence of life on Earth, let's keep it clean!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1011
EPA Comment ID: 20178
EPA Comment Code: 6120

Comment: take the rocket fuel out of our fuckin drinking water

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-1013
EPA Comment ID: 20179
EPA Comment Code: 6120

Comment: I urge the EPA to carefully examine the health effects of any level of Perchlorate in the nation's drinking water.

Response: See response to comment code 6120.

Commenter Name: P. & T. Lyon
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1014
EPA Comment ID: 20180
EPA Comment Code: 6120

Comment: PLEASE regulate perchlorate contaimination in drinking water. We are deeply disappointed in this administration's conservation and environmental record AND WE VOTED FOR YOU. At the least, our government needs to address the qualiity of water and protect future generations. The damage in the last century in the Great Lakes is now damage forever and becoming acceptable. IT IS NOT ACCEPTABLE.

I HATE MORE REGULATIONS BUT REGULALTE PERCHLORATE. The job of the federal government is to protect our nation, do it.

Response: See response to comment code 6120.

Commenter Name: Miguel A. Diaz
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1015
EPA Comment ID: 20181
EPA Comment Code: 6120

Comment: This is a request to ask you, to please Keep perchlorate out of our drinking water.

Thank you,

Miguel A. Diaz

Response: See response to comment code 6120.

Commenter Name: Ed Olmstead
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1016
EPA Comment ID: 20182
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water perchlorate contamination is a nationwide problem.

I do not, nor do I know if anyone can prvoe beyond a thin shadow of a doubt that perchlorate is harmful to life. However, when it comes to public good and the health of the country the fact that perchlorate is likely to be harmful in ways we know and don't know at this time is more than enough evidence to regulate this contaminant.

The job of the EPA is to protect the environment. The job the EPA is not to protect the corporations and the obscene corporate profits and practices that have led this country into a disastorous position financially and politically. I strongly urge you to work for the public good and give up the policies of the last eight years of protecting military/industrial complex at the expense of the US citizenry. A effective military does not have to be maintained at the expense of poisoning our own people. Do the right thing and regulate this poison in the environment.

Ed Olmstead 43 Stilson Ave Florence, MA 01062

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1018
EPA Comment ID: 20183
EPA Comment Code: 6120

Comment: The EPA is becomming a spot on this nations system. Instead of protecting the enirоment, they're safeguarding ways to further pollute our waters. When is this madness going to stop?

Response: This is not a comment, a response is not necessary.

Commenter Name: L. M. Maloney
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1021
EPA Comment ID: 20184
EPA Comment Code: 6120

Comment: I am not an organization. I am a mother and grandmother. I don't want my grandchildren drinking perchlorate. It is essential that the EPA maintain standards for drinking water that will protect our next generation from the kind of disasters we see happening in China. Can we preserve an environment fit for our children? Yes we can!

Response: See response to comment code 6120.

Commenter Name: Richard R. Quick
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1028

EPA Comment ID: 20185
EPA Comment Code: 6120

Comment: I support the regulation of perchlorate in drinking water. It should have happened a long time ago and the agencies responsible for allowing it into the water supply should have been stopped and disciplined a long time ago.

Why would anyone want the by products or components of rocket fuels in their water?

Richard R. Quick 15150 Warwick Detroit, Mi 48223

Response: See response to comment code 6120.

Commenter Name: Beth Robelia
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1033
EPA Comment ID: 20187
EPA Comment Code: 6120

Comment: To whom it may concern:

Your decision not to regulate perchlorate is irresponsible and will have tragic consequences for pregnant women and young children.

The 153 public water systems that are affected by this contamination will impact the lives of over 20 million people.

Please reconsider your decision. None of us would want to leave this sort of contamination for our children. I am sure none of the EPA personnel involved would want their children or grandchildren drinking water contaminated with perchlorate and you should not pretend that it would be OK for "other people."

Thank you for reconsidering your decision,

Beth Robelia, Ph.D.

Response: See response to comment code 6120.

Commenter Name: S. Randolph
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1034
EPA Comment ID: 20188
EPA Comment Code: 6120

Comment: I understand that the U.S. EPA issued a preliminary determination not to regulate perchlorate in drinking water. I urge you to reverse this determination.

The health risks particularly to the thyroid gland of children of even small amounts of perchlorate are severe enough to demand regulation.

Perchlorate contamination is not a rare event but has been found to be a nationwide problem.

Given the adverse health impacts of even lower levels than previously found problematic, it is essential that this contaminate be regulated to protect the public's health.

Response: See response to comment code 6120.

Commenter Name: P. Turner
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1036
EPA Comment ID: 20189
EPA Comment Code: 6120

Comment: NO PERCHLORATE in PUBLIC WATER ! ! !

How many ways can you spell poison?

Response: See response to comment code 6120.

Commenter Name: Anne Felosak
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1038
EPA Comment ID: 20190
EPA Comment Code: 6120

Comment: To those responsible for keeping our drinking water as healthy and free from contaminants as possible: I strongly urge you to reconsider letting any chemicals be given a pass as safe in our drinking water and even in the environment. We have to be more careful than ever about upsetting the balances in nature. Please keep our water as pure as possible. Anne Felosak

Response: See response to comment code 6120.

Commenter Name: S. Denmark
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1039
EPA Comment ID: 20191
EPA Comment Code: 6120

Comment: I am a private citizen and urge you to reverse the decision to not regulate perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Sara Dovre Wudali
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-1047
EPA Comment ID: 20192
EPA Comment Code: 6120

Comment: Hi,

I am concerned about perchlorate in drinking water. I would like to have faith that my tap water is as clean as we can make it. I'm worried about the potential health problems and growth problems linked to percholorate. Please consider regulating it.

Thanks, Sara Dovre Wudali St. Paul, MN

Response: See response to comment code 6120.

Commenter Name: Katie Giddings
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1051
EPA Comment ID: 20193
EPA Comment Code: 6120

Comment: My family and I drink tap water rather than bottled water because of the harmful environmental effects of plastic bottles and the wasted energy of shipping water in bottles. Please do not endanger our health by allowing poisons into our precious drinking water. I ask the EPA to regulate perchlorate in drinking water, along with any other substances that can cause harm and might be found in our water. The Environmental Protection Agency needs to begin living up to its name again rather than being the agency to eliminate needed protections.

Thank you.

Katie Giddings 27 Turner St #2, Salem MA

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1052
EPA Comment ID: 20194
EPA Comment Code: 6120

Comment: no no no! what is the matter with you people? do your job please, which is to protect me, not put me at risk.

thank you

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-1054
EPA Comment ID: 20195
EPA Comment Code: 6120

Comment: Dear EPA:

I've been working with communities over the past eight years to reduce pollutants in stormwater as required by Phase II of the Clean Water Act. Countless hours and dollars later, communities are making headway in cleaning up our surface waters. My region of the county gets its drinking water from the Detroit River, where I'm sure the industrial history of the area has deposited perchlorate into the Detroit River. Please join communities in protecting our water resources and regulate this dangerous chemical in our drinking water. You have required communities to minimize pollutants in our lakes and streams. Now please do your part in continuing our progress in protecting our drinking water.

Thank you.

Response: See response to comment code 6120.

Commenter Name: D. Knutson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1055
EPA Comment ID: 20196
EPA Comment Code: 6120

Comment: Keep perchlorate out of drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1057
EPA Comment ID: 20197
EPA Comment Code: 6120

Comment: To the decision makers at the EPA:

Perchlorate laced drinking water. Would YOU drink this? Would you let your KIDS drink this? PLEASE: DO YOUR JOB. If Bush prohibits you from doing it, please make HIM drink this. Thanks.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1061
EPA Comment ID: 20198
EPA Comment Code: 6120

Comment: Please don't allow Perchlorate in our Drinking Water: Preliminary Regulatory Determination on Perchlorate

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1065
EPA Comment ID: 20199
EPA Comment Code: 6120

Comment: I am writing to urge you to regulate the allowable limits of perchlorate in this nation's drinking water. With many safety questions still outstanding, this is a necessary step not only to protect the public health, but also to bolster public confidence in the ability of government regulators to take a stand against the interests of industry and act first in the best interest of the citizens of this country. Thank you.

Response: See response to comment code 6120.

Commenter Name: Fran Sugarman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1066
EPA Comment ID: 20200
EPA Comment Code: 6120

Comment: We are very concerned by the recently announced decision of the EPA to not regulate perchlorate in our drinking water. Perchlorate is an extremely harmful chemical used in rocket flares and explosives. We do not want to see our children exposed to this contaminant.

In the spirit of our new President- please listen to our concerns -and what parents want and reverse your decision.

Sincerely Fran Sugarman

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1067
EPA Comment ID: 20202
EPA Comment Code: 6120

Comment: May you suffer from the toxins which you permit in our drinking water.

Response: See response to comment code 6120.

Commenter Name: B. McCollum

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1068
EPA Comment ID: 20203
EPA Comment Code: 6120

Comment: The U.S. Environmental Protection Agency should reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Isn't this what your mission is about-- To protect the public and the environment from harmful contamination and pollution? Perchlorate contamination is a national problem and has severe health impacts that affect us all, especially the most vulnerable among us.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1072
EPA Comment ID: 20204
EPA Comment Code: 6120

Comment: What is the thinking here? Please act immediately and regulate Perchlorate in our drinking water.

Response: See response to comment code 6120.

Commenter Name: Peggy Rinard
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1075
EPA Comment ID: 20206
EPA Comment Code: 6120

Comment: Please reverse the EPA decision not to regulate perchlorate in drinking water.

Peggy Rinard 4469 Evergreen Drive St. Paul, MN 55127

Response: See response to comment code 6120.

Commenter Name: Patrick L. Doss-Smith
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1076
EPA Comment ID: 20207
EPA Comment Code: 6120

Comment: To whom it may concern,

Please reconsider the EPA's preliminary determination concerning regulation of Perchlorate levels in our drinking water. I am particularly concerned about potential damage to the thyroid in a developing fetus. As you may know, damage during development can lead to serious problems such as retardation, loss of hearing, etc. These sorts of issues are devastating to the individuals affected

and costly to our society. We must not let short term profits harm the long term health and well being of the ecosystem and subsequently, us. We need stronger regulation of Perchlorate.

Respectfully,

Patrick L. Doss-Smith

Response: See response to comment code 6120.

Commenter Name: B Seng
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1080
EPA Comment ID: 20208
EPA Comment Code: 6120

Comment: Please take action to regulate perchlorate in drinking water. At the very least you must have programs in place to measure the amounts in public drinking water systems so that consumers can know whether or not they are protected. This action will also spur water filter manufacturers to come up with solutions for consumers.

Response: See response to comment code 6120.

Commenter Name: B Ferguson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1081
EPA Comment ID: 20209
EPA Comment Code: 6120

Comment: Keep rocket fuel out of our drinking water. Reverse this decision.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1082
EPA Comment ID: 20210
EPA Comment Code: 6120

Comment: When are you going to stop killing us? We need drinkable water. Why are you doing this?

Response: This is not a comment, no response necessary.

Commenter Name: James W. Smith
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1083
EPA Comment ID: 20211
EPA Comment Code: 6120

Comment: We must not allow Perchlorate in our water. This chemical is harmful and must be regulated from all water used by our citizens. Thank you.

Sincerely, James W. Smith 821 Heritage Point Chesapeake, VA 23322

Response: See response to comment code 6120.

Commenter Name: E Paulson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1087
EPA Comment ID: 20212
EPA Comment Code: 6120

Comment: Please regulate the amount of perchlorate in our drinking water. It is harmful to the thyroid, the thyroid effects not only our metabolism, but our heart. My cousin a middle aged man of 52 has a heart which is only functining at 25%, because of damaged sustained from a dysfunctioning thyroid. The thyroid damage and heart damage has affected his life and family. Perchlorate is a highly reactive compound and considering the other organic chemical componds in our water, what other products will they be forming which will be effecting our bodies? Please reconsider and regulate this compond in our water. Thank you.

Response: See response to comment code 6120.

Commenter Name: E.E. Jumikis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1090
EPA Comment ID: 20213
EPA Comment Code: 6120

Comment: The recent decision by the Environmental Protection Agency not to issue standards for perchlorate in drinking water is a profligate flight from its regulatory responsibility. As a victim of oral cancer which has fried my thryroid, I am very sensitive to the effects of perchlorate on thyroid function and development. I understand how a lack of prescience can lead to disastrous consequences. As our children proliferate mental afflictions like ADHD, autism and other mental impairments, EPA must not abandon its responsibility to regulate perchlorate and other proven harmful chemicals in our drinking water.

Response: See response to comment code 6120.

Commenter Name: John Ganapes
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1093
EPA Comment ID: 20214
EPA Comment Code: 6120

Comment: I am writing to urge you to limit levels of Perchlorate in our drinking water to extremely low numbers. As a parent I am concerned about the health of my children and will not tolerate any risk to them at all.

John Ganapes Minneapolis MN 55407

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1095
EPA Comment ID: 20215
EPA Comment Code: 6120

Comment: EPA agrees that perchlorate has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher. Thus perchlorate contamination is a nationwide problem--and has health impacts at lower levels than previously thought.

Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development, and metabolism. Developing fetuses, infants, and children with thyroid impairment may suffer mental retardation, loss of hearing and speech, or deficits in motor skills.

As a mother and as an American, I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. This is not the time to take an unwarranted, dangerous step away from the mission of the Environmental Protection Agency to safeguard our citizens, young and old, from harmful containments in one of our country's most critical resources.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1096
EPA Comment ID: 20216
EPA Comment Code: 6120

Comment: SInce we say we care about our environment, lets do what we say and take action to deal with this toxin before it gets too late.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1097
EPA Comment ID: 20217
EPA Comment Code: 6120

Comment: This is a request for the U.S. EPA to reverse its preliminary decision not to regulate perchlorate in drinking water. Perchlorate can impair the thyroid gland and cause significant health risks to fetuses, infants and children. Perchlorate has been found in numerous water sources in the U.S. and the EPA should do its job and protect the public from such contamination.

Response: See response to comment code 6120.

Commenter Name: M. Hoover
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1098
EPA Comment ID: 20218
EPA Comment Code: 6120

Comment: Please reverse your preliminary determination regarding regulations for perchlorate in drinking water.

Perchlorate contamination is a problem across the country. It negatively impacts our health at lower levels that thought previously - with possible impairment to the thyroid. Of special concern is the impact on healthy thyroid function in fetuses, infants and children. Possible negative outcomes include mental retardation, hearing, speech and motor deficits.

Perchlorate contamination has been found in hundreds of sites, more than 35 states and over a 150 public water systems.

Regulation by the EPA provides a necessary mechanism to protect our health.

Response: See response to comment code 6120.

Commenter Name: Chris Jones
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1100
EPA Comment ID: 20219
EPA Comment Code: 6120

Comment: We do not want Perchlorate in our drinking water. If ground water has potential to be contaminated with Perchlorates then we need it monitored and evaluated.

Thank you Chris Jones

Response: See response to comment code 6120.

Commenter Name: H. Kitrosser
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1104
EPA Comment ID: 20220
EPA Comment Code: 6120

Comment: I am against your preliminary decision not to regulate perchlorate in drinking water. Please reconsider and keep our drinking water safe.

Response: See response to comment code 6120.

Commenter Name: Solo Greene
Commenter Organization: Nez Perce Tribe
EPA Document ID: EPA-HQ-OW-2008-0692-1106
EPA Comment ID: 20221
EPA Comment Code: 6120

Comment: Water is one of the most sacred things to Native Americans, and without clean, quality water, we as a people aren't going to be here very much longer. The animals, birds, fish, vegetation and natural resources are already suffering because of contaminated water, and we don't need any more of it entering our water ways, especially when we can avoid it. Please do not allow this to happen.

Response: See response to comment code 6120.

Commenter Name: J. Blakeley
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1110
EPA Comment ID: 20222
EPA Comment Code: 6120

Comment: Let's keep this pollutent out of our water!

Response: See response to comment code 6120.

Commenter Name: L.A. and S. Warner
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1115
EPA Comment ID: 20223
EPA Comment Code: 6120

Comment: Perchlorate does not belong in water, and it should be a right of every American to have drinking water free of chemical contamination. My family is suffering from autoimmune issues. We notice more and more people who are dealing with chronic health issues and strongly believe that our country's loose use of synthetic products could be to blame. Keeping perchlorate out of drinking water is a no brainer. Why don't we start here!

Response: See response to comment code 6120.

Commenter Name: M.A. Baier
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1116
EPA Comment ID: 20224
EPA Comment Code: 6120

Comment: no perchlorate in the drinking water/ regulate rocket fuel

Response: See response to comment code 6120.

Commenter Name: George Hasapidis
Commenter Organization: Cumberland Grange
EPA Document ID: EPA-HQ-OW-2008-0692-1120
EPA Comment ID: 20225
EPA Comment Code: 6120

Comment: Please protect humans and other animals from the harm that drinking perchlorate does. This is a known toxin, and it is the EPA's responsibility to protect us from it.

Response: See response to comment code 6120.

Commenter Name: J. Fredrick
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1121
EPA Comment ID: 20226
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

I live in Michigan and believe that perchlorate is in my drinking water. I have a thyroid problem that I suffer with for the last 2 1/2 years. I have no insurance and have to pay for specialist and perscriptions out of pocket.

Is your purpose in Washington to help save our viable drinking resources and the citizen's with which you represent?!

Response: See response to comment code 6120.

Commenter Name: Laurie Dixon
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1123
EPA Comment ID: 20227
EPA Comment Code: 6120

Comment: To whom it may concern,

It is crucial to my family as well as everyone I know that every measure be taken to protect our groundwater.

Living in Michigan, we have watched for decades upon decades as our environment has been decimated with toxic pollutiion. Everyone in this area lives near a "superfund" site.

This is a huge issue for citizens, probably more than any government agency realizes. Cancer has become a plague in southeast Michigan.

Please do everything possible, setting up whatever measures are needed to stop the contamination our water supply.

Sincerely, Laurie Dixon

Response: See response to comment code 6120.

Commenter Name: Renee Kaiser-Muelken
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1124
EPA Comment ID: 20228
EPA Comment Code: 6120

Comment: I strongly encourage the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

The EPA knows that perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought, and that a national primary drinking water regulation would provide a meaningful opportunity to protect public health. And we must be responsible to protect the most vulnerable in our society, the children - our future.

Thank you, Renee Kaiser-Muelken

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1125
EPA Comment ID: 20229
EPA Comment Code: 6120

Comment: The EPA must stop now the Bush administration's poisoning of our water, our environment, our lives. I am sure the appointed political leaders of the EPA can make a last gasp effort to enrich corporate leaders and others who benefit financially if the EPA allows percholate and other poisons in our water, but it will be a shortlived decision, and we will remember for a long time those who tried to slip one by us on their way out the door. For those of you who might allow this to happen, goodbye and good riddance.

Response: See response to comment code 6120.

Commenter Name: J. Dreifus

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1127
EPA Comment ID: 20230
EPA Comment Code: 6120

Comment: I think the EPA needs to reverse its position on regulating perchlorate. How can it not regulate this chemical?

Response: See response to comment code 6120.

Commenter Name: S. Eckes
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1128
EPA Comment ID: 20231
EPA Comment Code: 6120

Comment: Please, no perchlorate in drinking water.

Thanks.

Response: See response to comment code 6120.

Commenter Name: Phillip Lamoureux
Commenter Organization: Michigan State University
EPA Document ID: EPA-HQ-OW-2008-0692-1129
EPA Comment ID: 20232
EPA Comment Code: 6120

Comment: Please regulate perchlorate levels in drinking water, and work to prevent groundwater perchlorate contamination from industrial and government sources. We need very low, safe standards for this pollutant.

Sincerely, Phillip Lamoureux Biochemist and Cell Biologist Michigan State University

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0655
EPA Comment ID: 20233
EPA Comment Code: 6120

Comment: As a pediatrician, I think it is unwise to increase the allowed amount of perchlorate in the drinking water. The fetus and he growing child are more sensitive to toxins than adults and need protecting.

Response: See response to comment code 6120.

Commenter Name: T.J. Blair
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0656
EPA Comment ID: 20234
EPA Comment Code: 6120

Comment: It defies logic and common sense to dump toxic rocket fuel into or near drinking water sources. This practice will be especially harmful to people living near military bases. I urge you to SUPPORT OUR TROUPS, our children and others by NOT approving this regulation.

Thomas J. Blair 592 W. 2nd St. Winston-Salem, NC 27101

Response: EPA is not dumping toxic rocket fuel into or near water sources. Rather, EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Lynn Nadeau
Commenter Organization: HealthLink
EPA Document ID: EPA-HQ-OW-2008-0692-0657
EPA Comment ID: 20235
EPA Comment Code: 6120

Comment: Rocket fuel has no place in drinking water. Incidence of cancer rises as we allow our environment to be degraded. Please, EPA, protect us! Live up to your title!

Here in Massachusetts, we are well aware of the high rates of breast cancer on Cape Cod as well as the elevated amount of perchlorate in the water near the military base.

Response: See response to comment code 6120.

Commenter Name: Robin Mark Freeman
Commenter Organization: Merritt College
EPA Document ID: EPA-HQ-OW-2008-0692-0662
EPA Comment ID: 20236
EPA Comment Code: 6120

Comment: Eric Burneson Office of Ground Water and Drinking Water Standards and Risk Management U.S. Environmental Protection Agency

Dear Sir:

We the undersigned are concerned that EPA's failure to regulate perchlorate, as well as its unprotective proposed health reference level, will adversely affect the health and development of hundreds of thousands, perhaps millions of American children. It has taken EPA years, with its extensive resources, to come to its conclusions. Its findings are complex and controversial. We cannot afford to have this decision rushed out the door, in the waning days of the current administration, without giving impacted communities sufficient time to comment.

Response: See response to comment code 6120.

Commenter Name: L. L. Schumacher
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0664
EPA Comment ID: 20238
EPA Comment Code: 6120

Comment: Oct. 8, 2008

Leonard L. Schumacher 16516 Denise Dr. Austin, Texas 78717

U .S. Environmental Protection Agency Attn: Steve Johnson, EPA Administrator Arei1 Rios Building 1200 Pennsylvania Ave. N .W. Washington, DC 20460 Dear Mr. Johnson,

I have read recently about the toxic rocket fuel ingredient (perchlorate) that has been found in public water supplies at 395 sites in 35 states, and that the EPA does not intend to rid it from the water.

The levels found are high enough to affect thyroid function and pose developmental health risks, particularly for babies and fetuses according to some scientists. Great!!!

Combine this toxin with all the other pesticides, insecticides, and the other many dangerous toxins and chemicals in our food supply, no wonder people are getting cancer.

Response: This is not a comment, a response is not necessary.

Commenter Name: B. Raimondo
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0666
EPA Comment ID: 20240
EPA Comment Code: 6120

Comment: STop!!!! Perchlorate in the drinking water!!!

Response: See response to comment code 6120.

Commenter Name: Tatjana and Jeremy Thomas
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0669
EPA Comment ID: 20241
EPA Comment Code: 6120

Comment: Can't believe this has been going on for years. Is rocket fuel more important than human life? Of course we will just take some drugs to cover up the symptoms and keep doing what we are doing best, COVER UP THE BAD STUFF! God Bless America.

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0671
EPA Comment ID: 20244
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPAâ€™s refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

Perchlorate is a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children. The adverse effects of Perchlorate have not been extensively investigated. We do not know the full range of damage that this toxic chemical is having on our environment or our people. Nor have scientist looked at the synergistic effects of this poison, in combination with the thousands of other toxic substances known to be contaminating our drinking water. Not regulating this harmful chemical in our drinking water is unacceptable.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0671
EPA Comment ID: 20246
EPA Comment Code: 6120

Comment: How many more people must die or be severely impaired before EPA takes it's job of protecting the environment and the people of this country seriously. These harmful chemicals are poisons. Too many have already been harmed. It appears to those of us, who've been harmed by toxic chemicals that the EPA has sold our lives and health away to special interests and chemical companies. Too many people have already been harmed. It appears to those of us, who've been harmed by environmental and consumer by-product toxins that the EPA has sold our lives and health away to special interests and chemical companies. How is this any different than slave trafficking or child prostitution? Your failure to protect us indicates a wanton disregard for our lives!

I urge you to protect the environment, these current generations and the future generations of our country, in accordance with the Safe Drinking Water Act and protect all our health. Stop selling us out!

Response: See response to comment code 6120.

Commenter Name: P. Morello
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0674
EPA Comment ID: 20247
EPA Comment Code: 6120

Comment: You MUST regualte perchlorate under the Safe water Drinking Act...please.

This chemical is found in rocket fuel & is a big safety issue for the public & our environment. It is a very dangerous chemical. What is wrong with you that you are NOT outlawing this chemical to be found in America's drinking water?

Response: See response to comment code 6120.

Commenter Name: Judy F. Rosenblith
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0675
EPA Comment ID: 20248
EPA Comment Code: 6120

Comment: As a retired Professor whose specialty was child development and whose research involved newborns, I am particularly shocked by any lowering of standards for perchlorate that should be tightened. The effects on pregnant women and newborns are particularly important in informing my views. Please reconsider the current proposal.

Sincerely, Judy F. Rosenblith Prof. Emerita, Wheaton College (MA) judyrosenblith@earthlink.net

Response: See response to comment code 6120.

Commenter Name: D. Manzullo
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0676
EPA Comment ID: 20249
EPA Comment Code: 6120

Comment: How amazing that the health concerns of US Citizens continues to be put on the back burner by the Agencies that are supposed to be protecting us.

With tens of thousands of Thyroid Cancers diagnosed every year, how can we not be more pro-active in protecting our youth from unnecessary expense and health risks?

Response: This is not a comment, a response is not needed.

Commenter Name: Lisa Hampton
Commenter Organization: Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-0677
EPA Comment ID: 20251
EPA Comment Code: 6120

Comment: No perchlorate in my drinking water! This decision is harmful to public health, and the EPA's refusal to to set a drinking-water standard for perchlorate is deplorable. As you know, perchlorate has been linked to thyroid problems in pregnant women, newborns and young children. As someone who suffers from thyroid problems, exhaustion which stopped my life for the 13 years it took me to figure out what was going on, I can personally attest to how serious thyroid problems can be.

Response: See response to comment code 6120.

Commenter Name: Lisa Hampton
Commenter Organization: Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-0677
EPA Comment ID: 20252
EPA Comment Code: 6120

Comment: The Senate Environment and Public Works Committee has endorsed legislation requiring the EPA to set a federal standard for perchlorate and to monitor levels of the chemical in tap water. This I heartily support. We need to reduce the maximum safe levels for perchlorate as opposed to allowing them to be 15 times higher than they were in 2002.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0678
EPA Comment ID: 20253
EPA Comment Code: 6120

Comment: I feel the stricter the standard on perchlorate levels in drinking water, the better. There is no ambiguity in the science that tells us that perchlorate is extremely harmful to the health of humans, especially to children.

Response: See response to comment code 6120.

Commenter Name: S. Smolen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0679
EPA Comment ID: 20254
EPA Comment Code: 6120

Comment: Dear Sir,

I am writing to you in response to the EPA's preliminary descision not to set a national maximum contaminant level for perchlorate (Docket ID # EPA-HQ- OW-2008-0068). I am a former resident of the San Gabriel Valley, California, and US citizen whose family was exposed to contaminated groundwater containing perchlorate for a significant length of time. I was exposed to perchlorate at elevated levels through drinking water and also now suffer Hashimoto's thyroid disease. Following discovery of the profound levels of contamination in the San Gabriel Valley, I have been very discouraged and disappointed in the apparent lack of concern for residents whose health has potentially been affected by long-term, historic, contamination. I appreciate the efforts that have since been made to clean up the toxins and to protect the drinking water of current residents, but that does nothing for residents that have already been exposed. In addition, I now reside in a state that does not have a MCL for perchlorate despite having known perchlorate releases. I am concerned for my children as well as the public's safety. It is for these reasons that I am very concerned about the EPA's preliminary decision not to set a maximum contaminant level for

perchlorate. I worry that we are facing another situation where we will be looking back wishing more appropriate safety measures had been implemented.

Response: See response to comment code 6120.

Commenter Name: Marcia Willhite
Commenter Organization: Illinois Environmental Protection Agency
EPA Document ID: EPA-HQ-OW-2007-0068-0155
EPA Comment ID: 20257
EPA Comment Code: 6120

Comment: The Illinois Environmental Protection Agency ("EPA") recommends that the Agency reconsider its position of not regulating perchlorate, 2,4-dinitrotoluene, and 2,6-dinitrotoluene under the National Primary Drinking Water Regulation.

Response: This comment is outside of the scope of this action, no response necessary.

Commenter Name: Thomas Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0162
EPA Comment ID: 20267
EPA Comment Code: 6120

Comment: Perchlorate

Perchlorate is a very important issue for the drinking water community, and the perchlorate options detailed in the May 1st Federal Register notice raise many complex issues. Perchlorate provides EPA with a critical opportunity to appropriately implement the standard setting provisions of the 1996 SDWA amendments and the CCL/UCMR process. Additionally, there has been significant public interest generated by press coverage and subsequent interest by legislative bodies in certain states and at the federal level.

Building upon our position previously communicated to EPA in letters on February 2, 2005 and May 27, 2005, we recommend that EPA now make the decision to regulate perchlorate. AWWA believes that EPA has enough information to make a positive regulatory determination, and then to move forward with a proposed perchlorate regulation consistent with the requirements of the Safe Drinking Water Act.

We make this recommendation for the following reasons, absent any one of which we might make a different recommendation:

1. The National Research Council (NRC) and the Centers for Disease Control and Prevention (CDC) have found that perchlorate may have an adverse impact on the health of persons.

2. Perchlorate is known to occur in public water supplies in a number of states.

3. While occurrence data does not suggest that perchlorate occurs at levels of public health concern in the vast majority of public drinking water supplies and the population at risk appears to be small,

that group does include a sensitive subpopulation (pregnant women and developing fetuses) of significant concern.

4. The Greer data and the Reference Dose (RfD) recommended by the National Research Council (NRC) now make it possible for EPA to determine a protective level for perchlorate with a degree of confidence appropriate to a national primary drinking water regulation.

5. There are appropriate and reliable analytical methods for utilities and others to measure perchlorate concentrations in public water supplies, as documented by UCMR sampling, and laboratory capacity is not an issue.

6. A number of states are moving to regulate perchlorate and a patchwork of different regulations will confuse the public and the regulated community. And

7. Strong anecdotal data suggests that the lack of a perchlorate MCL has impeded a number of cleanups at hazardous waste sites. Cleanup at these sites could benefit public water suppliers, among others.

Response: See response to comment code 6120.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0166
EPA Comment ID: 20275
EPA Comment Code: 6120

Comment: The notice also discusses perchlorate and does not provide a regulatory determination for this contaminant despite the availability of extensive data and high public concern. Because of the high public concern there is also high political interest. As local stewards of public health, we believe that if perchlorate presents a public health risk, then EPA should establish a maximum contaminant level for it. AMWA believes strongly in the regulatory process outlined in the 1996 Amendments. In the case of perchlorate, AMWA believes that the information available to the agency clearly points to a determination to regulate.

It appears that the agency has deferred the decision on perchlorate based solely on wanting a more accurate determination of the relative source contribution that might be attributable to drinking water. The notice states that, absent that information, a determination whether setting a national primary drinking water standard would provide a meaningful opportunity to reduce risk for people served by public water systems cannot be made.

Response: See response to comment code 6120.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0166
EPA Comment ID: 20277
EPA Comment Code: 6120

Comment: At least nine states have addressed perchlorate through standards, health advisories, health based guideline levels, public advisories or other means. Utilities in states where no action has been taken face public perception and confidence problems at a minimum. EPA faces these same problems through continued inaction. A federal standard is needed in place of inconsistent state requirements.

AMWA urges EPA to keep in mind that a regulatory determination is the start of the regulatory process and not the end. Additional data is always gathered during the process. The final regulatory construct and requirements will be based on this data. All presently available data indicate that a positive determination is appropriate. Therefore AMWA believes that it is time for the regulatory process to begin. EPA can start this process outside the formal regulatory determinations and should do so. At minimum, a positive final determination should be made along with the determinations not to regulate 11 contaminants proposed in the present notice based on present data, and any additional information developed over the next several months while the agency's regulatory determinations are finalized.

If you have any questions about our comments, please do not hesitate to contact me or Erica Brown at 202-331-2820.

Sincerely, Diane VanDe Hei Executive Director Cc: Cynthia Dougherty, OGWDW

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1130
EPA Comment ID: 20290
EPA Comment Code: 6120

Comment: it is crucial to the health of our nation that we monitor perchlorate levels in our drinking water!

Response: See response to comment code 6120.

Commenter Name: Glen Shull
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1132
EPA Comment ID: 20291
EPA Comment Code: 6120

Comment: I don't know how much percholate is in our water but if it is in it we should regulate it. We did not regulate sub-prime loans, allowed people to submit loans to people who could not afford them and look what happened. If people are in danger of being sick from percholate, let's disallow it to be even close to illness causing levels. I teach tennis in Florida and drink a gallon of water a day, plus juices.

Glen shull

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1134
EPA Comment ID: 20292
EPA Comment Code: 6120

Comment: Do not permit perchlorate in water. Not healthful for babies, children or adults. If we are not to buy bottled water because of the environmental impact of plastic bottles then we need clean safe tap water to drink.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1139
EPA Comment ID: 20293
EPA Comment Code: 6120

Comment: On October 10, the EPA announced its preliminary decision not to regulate perchlorate in drinking water. EPA has requested comments from the public before making a final decision. Ask the Administration and the EPA to reverse this finding and regulate perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1141
EPA Comment ID: 20294
EPA Comment Code: 6120

Comment: I am writing to urge the EPA to regulate perchorate in our drinking water supplies. This is a chemical that has been proven to cause health problems, particulary in young children, and it crucial that we regulate it.

Thank you very much

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1144
EPA Comment ID: 20295
EPA Comment Code: 6120

Comment: Do not allow perchlorate in our water!!

Response: See response to comment code 6120.

Commenter Name: C. McFall
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1147
EPA Comment ID: 20296
EPA Comment Code: 6120

Comment: Perchlorate is only one of a cascade of foreign substances making its way into our drinking water. We are constantly learning of new, harmful substances whose interaction with our bodies and with other contaminates is unknown. The ONLY way we can preserve quality of our health as a nation is to ensure these foreign substances are not consumed by any of us. The EPA is supposed to PROTECT us from contamination, not facilitate it. This is our health, our future and our children we are talking about - not a group of hypothetical 'percentage of exposure' risks. Please wake up and start seeing our environment for the mess we have made it and help us clean it up, not add to the problem because someone talked you into it.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1152
EPA Comment ID: 20297
EPA Comment Code: 6120

Comment: Please reverse decision to allow perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Amy Cobaugh
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1153
EPA Comment ID: 20298
EPA Comment Code: 6120

Comment: Please regulate perchlorates in our drinking water. As a citizen, I am very concerned about the health affects on my children, who are especially vulnerable to pollutants.

Thanks,

Amy Cobaugh San Mateo County, CA

Response: See response to comment code 6120.

Commenter Name: Rebecca Teal
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1157
EPA Comment ID: 20299

EPA Comment Code: 6120

Comment: Please keep rocket fuel in my drinking water. I like the way it makes my third eye glow. Regards, Rebecca Teal

Response: This is not a comment; no response is necessary.

Commenter Name: J. Vasconcellos
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1158
EPA Comment ID: 20300
EPA Comment Code: 6120

Comment: Its time to be proactive, as well as foresighted. Whats easier and more desirable to treat: perchlorate in our drinking water or askewed thyroid disease in our children? Think the Future!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1162
EPA Comment ID: 20301
EPA Comment Code: 6120

Comment: We Minnesota voters just announced loud and clear in yesterday's vote that we're willing to pay higher taxes in return for increased protection of our water, air, and other natural resources. Let's bring our regulatory protection up to speed. Monitor Perchlorates.

Response: See response to comment code 6120.

Commenter Name: G. A. Bagazinski
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1166
EPA Comment ID: 20302
EPA Comment Code: 6120

Comment: No Percholate in Drinking Water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1167
EPA Comment ID: 20303
EPA Comment Code: 6120

Comment: how about trying to keep perchlorate to a minimum level in our drinking water, like around none would be good, yes?

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1169
EPA Comment ID: 20304
EPA Comment Code: 6120

Comment: Don't see any reason that we should have Perchlorate in our water. Please consider limiting it.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1171
EPA Comment ID: 20305
EPA Comment Code: 6120

Comment: Reverse your ruling on perchlorate. No one wants to drink something that is tainted with fuel ingredients The environmental impact of increased bottled water consumption should be a factor in your consideration. Every effort should be made to increase the purity of our drinking water, so we can help reduce the environmentally damaging, excessive consumption of bottled water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1177
EPA Comment ID: 20306
EPA Comment Code: 6120

Comment: I strongly believe the U.S. Environmental Protection Agency must reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Perchlorate is a serious concern health-wise, and I do not want it in the water I am drinking.

Response: See response to comment code 6120.

Commenter Name: Louise McEvers
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1180
EPA Comment ID: 20307
EPA Comment Code: 6120

Comment: As a citizen with low thyroid, I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Perchlorate contamination is a national problem that could impact many Americans.

Please reconsider your position.

Louise McEvers Austin, TX 78729

Response: See response to comment code 6120.

Commenter Name: K. Moreland
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1183
EPA Comment ID: 20308
EPA Comment Code: 6120

Comment: Percholate is a dangerous chemical and needs to be kept out of our drinking water. You must regulate this dangerous chemical

Response: See response to comment code 6120.

Commenter Name: Deb Arnason
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1184
EPA Comment ID: 20309
EPA Comment Code: 6120

Comment: Please do not allow percolate in our drinking water. Sadly. the EPA has deteriorated over the past 8 years. With our new President, I hope we can look forward to your PROTECTION that has been lacking by regulating this hazardous chemical as well as many others in our air, water and food supplies. Thank you for returning to sanity. Please help by doing the job we used to trust you for.

Deb Arnason 12 Dill St, Alva, FL 33920 386-288-4454 diamondteldeb@aol.com

Response: See response to comment code 6120.

Commenter Name: W. Mcclure
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1190
EPA Comment ID: 20310
EPA Comment Code: 6120

Comment: Please reverse your decision and keep perchlorate out of the water supply. The public health takes precedence over business convenience and cost.

Response: See response to comment code 6120.

Commenter Name: C. Rongstad

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1191
EPA Comment ID: 20311
EPA Comment Code: 6120

Comment: I ask the EPA to reverse its decision not to regulate perchlorate in drinking water. Why not regulate a chemical that has health impacts at low levels and is detectable in our drinking water?

Please consider the lack of regulation as harmful to the public and include perchlorate in drinking water regulations.

Response: See response to comment code 6120.

Commenter Name: T. J. Sanders
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1192
EPA Comment ID: 20312
EPA Comment Code: 6120

Comment: Let us do what it takes to save our environment and our planet. It is the only home we have. We are becoming over populated, and it is no longer acceptable to add toxins to our ater and air.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1195
EPA Comment ID: 20313
EPA Comment Code: 6120

Comment: Do not put perchlorate in our drinking water.

Thank you.

Response: See response to comment code 6120.

Commenter Name: Frances Ann Leary
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1209
EPA Comment ID: 20314
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

A national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Take the precautionary approach, or we will all pay later. It's harder to remove contaminants and try to make ammends with families impacted both emotionally and financially by the ramifications of toxics in their water. Now is the time to be a leader on this and other critical environmental issues.

Sincerely, Frances AnnLeary

Response: See response to comment code 6120.

Commenter Name: L. Thorpe
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1221
EPA Comment ID: 20315
EPA Comment Code: 6120

Comment: Please keep chemicals out of our water. It is harming my families health and yours.

Response: See response to comment code 6120.

Commenter Name: Shawn Taylor
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1231
EPA Comment ID: 20335
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. I believe this is urgent for public safety.

Sincerely,

Shawn Taylor

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1232
EPA Comment ID: 20336
EPA Comment Code: 6120

Comment: As a concerned citizen with a family living by a major river and atop an already imperiled aquifer, I am distraught that EPA is even considering not regulating perchlorate levels in the water supply. How can my government be so unconcerned for its citizens' well-being? Perchlorate is a component in rocket fuel, and the science shows that even in low amounts it can be a threat to our health.

It is no favor to industry for the EPA not to set safety levels and monitor water for the presence of perchlorate. Should contamination at unsafe levels occur, the damage to the health of even a few citizens, much less to the large numbers who might be affected in any significantly populated area, would be a terrible blow to the industry as well.

It should be very clear that wise regulation is good for everyone. This is EPA's obligation, the very reason for your existence. This is not a quasi-market situation in which if one party fails, someone else will step in. EPA is our last best defense against man-made environmental hazards. We the citizenry are counting on you.

Response: See response to comment code 6120.

Commenter Name: Patricia A. Gozemba
Commenter Organization: Salem Alliance for the Environment (SAFE)
EPA Document ID: EPA-HQ-OW-2008-0692-1234
EPA Comment ID: 20337
EPA Comment Code: 6120

Comment: We have seen our water supply for the City of Salem, MA jeopardized at Wenham Lake. We believe that the EPA should hold the line on weakening standards. I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; a national primary drinking water regulation would provide a meaningful opportunity to protect public health. The EPA should hold off on making determinations such as this until the new administration takes office.

Dr. Patricia A. Gozemba

Salem, Massachusetts

Response: See response to comment code 6120.

Commenter Name: Tony Dewalt
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1235
EPA Comment ID: 20338
EPA Comment Code: 6120

Comment: please remove rocket fuel, flare chemical from our waters. lets keep usa,s waters ahead of most of the worlds in drinking quality thank you tony dewalt

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1237
EPA Comment ID: 20339
EPA Comment Code: 6120

Comment: I have a chronic health condition and live not far from launch pads. The people of the community have long time wondered if the contaminants to which we are exposed are regulated or responsible for health issues. I am afraid as are those who read about perchlorates . We know they are not good for us! Please reverse the decision not to monitor this chemical and let us know you truly do care about the health of the public. It is critical to our childrens growth and the general health of our people.

Response: See response to comment code 6120.

Commenter Name: M. Musgrave
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1240
EPA Comment ID: 20340
EPA Comment Code: 6120

Comment: "Researchers at the Centers for Disease Control and Prevention (CDC) have just released findings that show that American women -- and especially women with low iodine intake -- are at risk of hypothyroidism due to common exposure to the toxin perchlorate. " I'm not making this up. Check the facts. Perchlorate must be regulated to protect us--that's your job! If you want to keep it do it better and reverse this ruling. Our new administration will be sure to make you accountable for your responsibilities to The People!

Response: See response to comment code 6120.

Commenter Name: T. Lampert
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1241
EPA Comment ID: 20341
EPA Comment Code: 6120

Comment: No relaxing of standards for water purity. No percholates inthe water!!!!!!!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1246
EPA Comment ID: 20342
EPA Comment Code: 6120

Comment: I am concerned about rocket fuel being in our water supply and wouldn't like it to be in it, please.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-1249
EPA Comment ID: 20343
EPA Comment Code: 6120

Comment: Please test for perchlorate in our drinking water!

Response: This regulatory action does not affect testing requirements for perchlorate. Please See response to comment code 6120.

Commenter Name: Cara Cordoni
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1250
EPA Comment ID: 20344
EPA Comment Code: 6120

Comment: Please protect our drinking water. Test for and protect us from percholate! Jet fuel is not food, not nutrition, not health and does not belong in our water or bodies. Please protect our babies, our children, our elderly. Do not make the same kind of mistake the FDA made with the pesticide that is killing our bees - protect us from the beginning.

Cara Cordoni

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1262
EPA Comment ID: 20345
EPA Comment Code: 6120

Comment: 3M has been dumping this chemical and several others in our aquifer for years. At first they said there were no negative effects from it, but later I believe concerns about cancer, possibly, have been raised.

At any rate, chemicals other than minerals supplied naturally are not a desirable item in potable water.

Please take care of this.

Thanks.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1264
EPA Comment ID: 20346
EPA Comment Code: 6120

Comment: What? Is not the the EPA the Environmental PROTECTION Agency? What is more important than monitoring and regulating what poisonous chemicals might enter our water sources? And what better motivation is needed than to protect our children? Our seeds of the future!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1265
EPA Comment ID: 20347
EPA Comment Code: 6120

Comment: Please do your job and keep our water safe. Keep Perchlorate out of the water

Response: See response to comment code 6120.

Commenter Name: N. Henderson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1266
EPA Comment ID: 20349
EPA Comment Code: 6120

Comment: As the mother of an infant, I urge the EPA to reconsider its position on the regulation of perchlorate in drinking water. Each and every contaminant in our public water supply jeopardizes the health of the citizens of this country, particularly are most vulnerable population--infants and children. Ultimately, a decision not regulate a chemical that we ingest has high financial cost when one 1 in 4 Americans will develop cancer during their lifetime. Please consider this factor when assessing this decision.

Response: See response to comment code 6120.

Commenter Name: Robert L. Oldershaw
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1268
EPA Comment ID: 20350
EPA Comment Code: 6120

Comment: Please get with the new program: emphasis on protecting the ENVIRONMENT rather than on protecting the excess profits of influencial corporations.

Please ask yourselves whether you need to regain some integrity and self-esteem before you leave for new jobs.

Thanks,

Robert L. Oldershaw

Response: See response to comment code 6120.

Commenter Name: Nancy B. Kurtz
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1269
EPA Comment ID: 20351
EPA Comment Code: 6120

Comment: Coming from a family that has a tendency toward environmentally triggered diseases I want to tell you to take responsibility and mandate the perchlorate out of our drinking water. We have only begun to realize how many diseases are triggered by contaminants and need to nip this track in the bud. This is a can of worms you don't want to be a part of opening.

Nancy B.Kurtz

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1271
EPA Comment ID: 20352
EPA Comment Code: 6120

Comment: I am speaking against the EPA's preliminary decision not to regulate perchlorate in drinking water. I'd like to believe the EPA is working primarily to protect the public's health and not catering to big industry's concerns that regulations hamper their ability to make money. The USA needs to be a world leader in protecting the environment with very stringent rules.

Response: See response to comment code 6120.

Commenter Name: Amy Rice-O'Rourke
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1274
EPA Comment ID: 20353
EPA Comment Code: 6120

Comment: Dear Ones,

As a working Mother who grew up swimming and fishing in Lake St. Clair, & one who I takes our own kids there all summer, I am very concerned about these new laxxed regulationsabout the amount of perchlorate in our drinking water. What is an exceptable amount of poisin? How long will it be until my children or their children show the effects of these pollutants? I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; a national primary drinking water regulation would provide a meaningful opportunity to protect public health. As you make these determinations, please bear in mind my 7 & 9 year old boys, their potential children and the hundreds of thousands of

other children who grow up all around the Great Lakes States & Canada and we deserve clean water to drink. We have to protect their legacy as well as their health.

Sincerely,

Amy Rice-O'Rourke

Response: See response to comment code 6120.

Commenter Name: J. M. Meyerson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1275
EPA Comment ID: 20354
EPA Comment Code: 6120

Comment: Please work hard keep contaminants like Perchlorate out of our drinking water. As citizens, we depend on you to protect us all.

Thank you,

Response: See response to comment code 6120.

Commenter Name: C. W. Doppler
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1280
EPA Comment ID: 20355
EPA Comment Code: 6120

Comment: Clean water is a basic human right and a basic government responibility. As a citizen, I demand that you regulate perchlorate contamination in our drinking water.

Christina W Doppler

Crown Point IN

Response: See response to comment code 6120.

Commenter Name: Gary Kropilak
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1281
EPA Comment ID: 20356
EPA Comment Code: 6120

Comment: Gary Kropilak

16 Peek St

Rochelle Park, NJ 07662

To whom it may concern,

Your decision to allow percholate to remain in our drinking water is unacceptable. Our limited supply of drinking water must be protected and free of all harmful contaminates. Even miniscule amounts of percholate can threaten the health of fetuses, infants, teens and adults. I implore you to REVERSE your decision not to regulate percholate. Please protect us.

Thank You,

Gary Kropilak

Response: See response to comment code 6120.

Commenter Name: S. Brown
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1284
EPA Comment ID: 20357
EPA Comment Code: 6120

Comment: I'm writing to ask the agency to reconsider its decision on the need to regulate perchlorate levels in drinking water. Given its widespread contamination (37+ states) and thyroid effects at low concentrations, particularly in utero, it is vital that the agency moves to protect public health.

Response: See response to comment code 6120.

Commenter Name: G. Guthmiller
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1285
EPA Comment ID: 20358
EPA Comment Code: 6120

Comment: Please regulate the perchlorate level in our drinking water. We do not need any chemicals dissolved in our water. We may find in the future that this chemical has many hazardous risks for humans. Please don't poison our future generations. Thank you.

Response: See response to comment code 6120.

Commenter Name: Susan D. Snyder
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1288
EPA Comment ID: 20359
EPA Comment Code: 6120

Comment: Re: Drinking water standards & Perchlorate: I find it ironic that the agency responsible for the safety and protection of both the American public and the national environment would consider that any amount of perchlorate - which is not a naturally occurring chemical - has an

acceptable level in the potable water of any mammal, whether human person or animal. To set any sort of standard/acceptable amount for percholorate presence is immoral, should never become legal and is, in the event, reprehensible. I understand that maintaining pure (perchlorate-free) water carries a cost: but it is nothing to the deep harm the chemical does to those who have no option but to drink it. Please, take the "high road" of consumer and environmental protection - in accordance with your mandate - and do not institutionalize the further poisoning of our water system. I would appreciate a written acknowledgment of my comment.

Susan D. Snyder 8628

Garfield Street

Bethesda, MD 208187

sue_snyder@verizon.net

Response: See response to comment code 6120. EPA acknowledges your request for a reply to your comment; however, EPA is unable to reply directly to all comments submitted.

Commenter Name: J. Kayle
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1291
EPA Comment ID: 20360
EPA Comment Code: 6120

Comment: Of course you need to regulate whether or not perchlorate is getting into our water supply! Don't be ridiculous. Please.

Response: See response to comment code 6120.

Commenter Name: Greg Swanson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1293
EPA Comment ID: 20361
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

On October 10, the EPA announced its preliminary decision not to regulate perchlorate in drinking water. I cannot understand why your agency would ever consider not regulating this contaminate. The purpose of your agency is to be the watchgard for the public in Protecting us from harmful substances. You need to side with the publics best interest in mind. If this causes manufacturers and industry to incur costs then they need to be responsible and include them in their cost of doing business just like all other repsonsible companies and manufactures.

Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; A national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Perchlorate is a harmful chemical used in rocket fuel, flares, and explosives. Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills. EPA agrees that perchlorate has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher.

Reverse your preliminary determination and responsibly regulate this potentially harmfull substance.

Thank You

Greg Swanson

Response: See response to comment code 6120.

Commenter Name: Kate Mendeloff
Commenter Organization: University of Michigan, Ann Arbor
EPA Document ID: EPA-HQ-OW-2008-0692-1294
EPA Comment ID: 20362
EPA Comment Code: 6120

Comment: I am a private citizen who has great concern about the potential pollution of our drinking water by perchlorate. Please be responsible for the general welfare and make this illegal!

Kate Mendeloff, University of Michigan, Ann Arbor

Response: See response to comment code 6120.

Commenter Name: Lisa Stewart
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1300
EPA Comment ID: 20363
EPA Comment Code: 6120

Comment: Please reverse your decision and regulate perchlorate in drinking water. Isn't potable drinking water a priority?

You need to shed your "too little too late" image of post 911 and show Americans that you are doing your job to protect us from contaminates either in the air or water.

Your attention to the this is vital to the well being of countless Americans.

Most sincerely,

Lisa Stewart

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1301
EPA Comment ID: 20364
EPA Comment Code: 6120

Comment: I first read about perchlorate in the newspaper several years ago when it was discovered to be on organic lettuce grown in California! PLEASE reverse your preliminary determination on setting a regulation for perchlorate in drinking water. This is a national problem - clean it up!

Response: See response to comment code 6120.

Commenter Name: J. Seegmiller
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1302
EPA Comment ID: 20365
EPA Comment Code: 6120

Comment: Keep perchlorate out of our drinking water.

Response: See response to comment code 6120.

Commenter Name: Lisa Quartararo
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1303
EPA Comment ID: 20366
EPA Comment Code: 6120

Comment: Perchlorate should be federally regulated just like any other chemical that has the potential to harm people or the planet. I don't understand what you are thinking!

Sincerely,

Lisa Quartararo

Colonia, NJ 07067

Response: See response to comment code 6120.

Commenter Name: Greta Mackenzie
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1307
EPA Comment ID: 20367
EPA Comment Code: 6120

Comment: since my drinking water comes from a surficial aquifer within a watershed affected by miami international airport, and concievable by the old aerojet facility, I would appeciate knowing it is safe to drink. Unfortunately the EPA dosnt inspire the confidence it used to under the Clinton administration. As far as I'm concerned, the more regulation on MCL's for water (and while we are at it air and food) the better!

greta Mackenzie PhD.

Response: This is outside of the scope of this effort, no response is necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1309
EPA Comment ID: 20368
EPA Comment Code: 6120

Comment: Please reverse your action to not regulate perchlorate in our drinking water. It's absurd that you would even consider allowing it in our drinking water----I mean you have to drink this water as well. Lets use some common sense.

Response: See response to comment code 6120.

Commenter Name: L. Doggett
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1310
EPA Comment ID: 20369
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: M. Hough
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1312
EPA Comment ID: 20370
EPA Comment Code: 6120

Comment: I am deeply concerned with regard to articles I have read regarding perchlorate in our drinking water. This is an issue I feel needs to be addressed by the EPA. It clearly is a harmful chemical which can impair the thyroid gland and affect fetuses, infants and children. This is dangerous even in the smallest amounts. The EPA has decided not to move forward to regulate perchlorate in drinking water which possibly will be a big mistake. You have your findings and you must act accordingly. This contamination in drinking water is nationwide and not to take the proper measures to ensure the safety of our drinking water would be harmful in the long run. Please reconsider and take the precautionary measures.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1313
EPA Comment ID: 20371
EPA Comment Code: 6120

Comment: I've been drinking water for a long time. My family drinks water. My pregnant daughter is passing the contents of the water she drinks on to her unborn child. Moreover, I believe the agents of our government responsible for water quality oversight drink water. In short, we all have a stake in keeping our water sources pure. Please keep faith with the trust we have put in you. Keep perchlorate out of our water (yours and mine). Reverse this decision.

Response: See response to comment code 6120.

Commenter Name: A. Crane
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1317
EPA Comment ID: 20372
EPA Comment Code: 6120

Comment: Attention EPA Officials: I don't want perchlorate in our water systems. What would Ralph Nader say if he heard you were stopping your testing of this dreadfully harmful chemical in our drinking water? I think he'd say "get back on it!" Please help keep our waters safe for all the plants, animals and people who can't live without it.

Thank you,

A. Crane

Response: See response to comment code 6120.

Commenter Name: Christy Anderson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1318
EPA Comment ID: 20373
EPA Comment Code: 6120

Comment: To whom it may or may not concern,

I strongly urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought. It is unethical and inappropriate to allow toxic substances in our drinking water; however, a national primary drinking water regulation would provide a meaningful opportunity to protect public health. Please protect our health and the health of our children!!

Christy Anderson

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1319
EPA Comment ID: 20374
EPA Comment Code: 6120

Comment: I urge the U.S. E.P.A. to reverse its preliminary determination on setting a regulation for perchlorate in drinking water as this can be very hazardous to large groups of our population and cannot be ignored.

Response: See response to comment code 6120.

Commenter Name: Heidi Washburn
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1322
EPA Comment ID: 20375
EPA Comment Code: 6120

Comment: To the EPA, As a citizen, parent, grandparent, and teacher, I strongly urge the EPA to reverse its decision NOT to regulate perchlorate, rocket fuel, in our nations water and drinking water. Perchlorate is a harmful chemical whose devastating effects on humans and animals will last generations. As a government organization created to protect our environment, I believe it is your moral duty to act now to insure that perchlorate does not make its way into the water. PLEASE ACT NOW --- KEEP PERCHLORATE OUT OF AMERICA'S WATER.

Respectfully submitted,

Heidi Washburn

4615 Daventry Place

Valrico, FL 33596

Response: See response to comment code 6120.

Commenter Name: Frank Blaskowitz
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1323
EPA Comment ID: 20376
EPA Comment Code: 6120

Comment: The EPA regulates a number potential health hazards. Perchlorate contamination is real and must be addressed. I urge the EPA to regulate this contaminant as quickly as possible.

Thank You,

Frank Blaskowitz

Response: See response to comment code 6120.

Commenter Name: Robert Prato
Commenter Organization: Bucks County HIRT
EPA Document ID: EPA-HQ-OW-2008-0692-1327
EPA Comment ID: 20377
EPA Comment Code: 6120

Comment: I would strongly urge the EPA to reconsider the perchlorate regulation for drinking water standards. I have experience with these chemicals first hand (I am a Captain on a regional Hazardous Material response team), and I have a great understanding of the short and long term effects of this type of chemical. Even minute amounts of this can cause harm to humans and animals alike. Please give due consideration to creating a standard for these chemicals.

Thank you.

Robert Prato Capt.

89-1 Bucks County

HIRT Bucks County, PA

Response: See response to comment code 6120.

Commenter Name: Maureen Roddy
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1328
EPA Comment ID: 20378
EPA Comment Code: 6120

Comment: Keep rocket fuel out of our drinking water!!! Our children are suffering from an epidemic of frontal lobe disorders -- autism is just one of them. Clean up our water and keep neurotoxins out. thank you.

Maureen Roddy

978 Van Auken Circle

Palo Alto, CA 94303

Response: See response to comment code 6120.

Commenter Name: Anonymous

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1329
EPA Comment ID: 20379
EPA Comment Code: 6120

Comment: Safe Drinking Water is one of the main indicators of a developed country. Allowing percholate do go untested or regulated in our country's municipal waters is a mistake - one that every citizen will unknowingly make when they reach for a glass of tap water. With so much effort being made to turn people away from the fallacy of bottled water, why would we give people any more reason to doubt their local water sources?

Please consider testing water for percholate and making sure levels are well below the permissible amount!

Response: This regulatory action does not affect testing requirements for perchlorate in local jurisdictions. Please see the response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1333
EPA Comment ID: 20380
EPA Comment Code: 6120

Comment: I urge the EPA to reverse its decision on Perchlorate. Thank you.

Response: See response to comment code 6120.

Commenter Name: John and Barb and family Harburg
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1334
EPA Comment ID: 20381
EPA Comment Code: 6120

Comment: Please keep perchlorate out of the water.

Thank you

John and Barb Harburg and family

Response: See response to comment code 6120.

Commenter Name: Julie Seifert
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1336
EPA Comment ID: 20382
EPA Comment Code: 6120

Comment: Please urge tj=he EPA to reverse it's preliminary determination on setting a regulation for permitting perchlorate in our drinking water. No levels are safe and we need to be protected!!!!!!!!!!!!!

Julie Seifert

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1337
EPA Comment ID: 20383
EPA Comment Code: 6120

Comment: Regulate Perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: D. Puyanic
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1339
EPA Comment ID: 20384
EPA Comment Code: 6120

Comment: You must regulate perchlorate - an ingredient in rocket fuel. You must reverse this finding and regulate perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Julia Burch
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1340
EPA Comment ID: 20385
EPA Comment Code: 6120

Comment: I do not want my drinking water standards loosened, especially when it comes to perchlorate. I understand that President Bush is trying to undo many important regulations that protect public health and our environment in his last few days in office. But EPA serves the American people, not just the President. EPA's job is to protect the public from harmful exposures whether acute or chronic. As well as to protect the environment for future generations. In the past eight years EPA has fallen down on this job. Regulations should be just as difficult to undo as they are to put in place to prevent politics and industry from having inappropriate influence on our nation's environmental health. Keep perchlorate out of our water. In addition, EPA needs to develop standards for atrizine as well. Pesticides should not be in our water either. And if the technology does not exist to remove these chemicals from drinking water then they should be banned from use or production.

Private Citizen Julia Burch 846 32nd Street Sarasota, Florida 34234

Response: Regarding regulation of perchlorate, See response to comment code 6120. Regarding regulation of atrazine, this is outside of the scope of this effort.

Commenter Name: Chip Thomas
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1344
EPA Comment ID: 20386
EPA Comment Code: 6120

Comment: Please reverse the decision to not regulate perchlorate. It needs to be regulated due to its potential harm.

Chip Thomas Tampa, Fl 813-238-0437

Response: See response to comment code 6120.

Commenter Name: Aaron Smith
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1346
EPA Comment ID: 20387
EPA Comment Code: 6120

Comment: To Whom It May Concern:

The decision to put into place measures to regulate perchlorate in drinking water rest on the EPA's assessment of potential reduction of public health risk caused by the pollutant. It seems logical to me, and I hope to you, that if there exists ANY risk, or even the possibility of a risk to an population of American people, no matter how small, that regulation is necessary. If the EPA concludes that even a small sub-population is affected by perchlorate, then the EPA is saying, in their opinion, it is okay to have polluted drinking water as long as it only hurts a few. I believe this is bad policy and hope that you would agree. Second, Drinking water is an extremely valuable resource, and will become more valuable in the coming decades. Water tables all over the world are falling, climate change is causing drastic changes to our sources of drinking water, and skyrocketing world population is going to make drinking water more and more of a scare resource in the decades to come. It is imperative that we protect our drinking water against all possible contaminates.

Thank you for you time and attention to this issue.

Aaron smith aaronsmith@alumni.utexas.net

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1351
EPA Comment ID: 20388
EPA Comment Code: 6120

Comment: Please do not let perchlorate into our drinking water.

Response: See response to comment code 6120.

Commenter Name: Marilyn Alvey
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1352
EPA Comment ID: 20389
EPA Comment Code: 6120

Comment: To Whom it may concern, Please strengthen standards for our drinking water. Why would anyone in their right mind allow toxic substances to be in water that US citizens are relying on to be safe and pure. We are the only civilized country that even puts chlorine in our drinking water, which is suspected of causing health problems, and is being looked at as a major player in the increase of breast cancer. We are so behind other nations in taking a proactive stance against toxins in our food, water and consumer goods. When are we going to wake up? Canada has just banned bisphenol A,as have most civilized countries, yet our government is still telling us that it is safe- NOT! It is in liners of all canned goods, so how does one avoid it? We all can't grow and can our own food, we rely on the government to set safety standards and my government is sadly behind the curve. Please do not allow perchlorate in our drinking water. Sincerely, Marilyn Alvey

Response: See response to comment code 6120.

Commenter Name: Marni Hall
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1353
EPA Comment ID: 20390
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse it's preliminary determination on setting a regulation for perchlorate in drinking water. It is irresponsible to ignore the fact that perchlorate has health impacts and if it is in our drinking water we are all at risk and suffer the impacts to our health. Please embrace this opportunity to protect public health. Sincerely, Marni Hall

Response: See response to comment code 6120.

Commenter Name: S. M. Gagnon
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1354
EPA Comment ID: 20391
EPA Comment Code: 6120

Comment: I am very unhappy with the EPA's preliminary decision not to regulate perchlorate in drinking water. The EPA must reverse this finding and regulate perchlorate in drinking water so as to protect the smallest, most vulnerable members of our society -- our babies and children. Clean, safe drinking water should be the right of every American.

Response: See response to comment code 6120.

Commenter Name: Francoise LaMonica
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1356
EPA Comment ID: 20392
EPA Comment Code: 6120

Comment: The health effects from ingesting low dosage perchlorate-contaminated water are not well known. But it's already known that it interferes with the body's iodine intake, causing an inhibition of human thyroid production. Regulation of this contaminent is clearly within the mission and mandate of your agency to protect humal health.

Further, since ammonium perchlorate which is used in solid rocket engine fuels has a limited shelf life and must periodically be replaced, a safe method of disposing of the chemical has to be designed and implemented. We cannot allow the buildup of perchlorate, notably in the Colorado Bassin, to continue unabated.

I urge you to reconsider your agency decision not to regulate this chemical.

Sincerely,

Francoise LaMonica 944 Centre Street Newton, MA 02459

Response: Please see the response to comment code 6120. Regarding commenter's statement "…since ammonium perchlorate which is used in solid rocket engine fuels has a limited shelf life and must periodically be replaced, a safe method of disposing of the chemical has to be designed and implemented", proper disposal of ammonium perchlorate falls outside of the scope of this regulatory action, as the Safe Drinking Water Act's authority is focused on whether or not the contaminant can be in public water systems.

Commenter Name: T. Greenlee
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1357
EPA Comment ID: 20393
EPA Comment Code: 6120

Comment: I am appalled at the idea of drinking a rocket fuel additive. I implore you regulate Perchlorate strictly.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1365
EPA Comment ID: 20394
EPA Comment Code: 6120

Comment: Please protect our water from being contaminted by preventing perchlorate to be in our water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1368
EPA Comment ID: 20395
EPA Comment Code: 6120

Comment: Are you retarded?

Anything and everything that is man made should be monitored, even it if is not adherently bad for people or the environment.

Please reconsider or the consequences will be dire.

Sincerely,

A concerned citizen

Response: See response to comment code 6120.

Commenter Name: Shannon No surname provided
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1371
EPA Comment ID: 20396
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. I personally do not want myself or my children to drink water that has a known contaminant that can effect thyroid function. I am actually not even sure why we would need to urge your decision in this direction as any chemical in our water system is alarming and should be regulated.

Thank you for your consideration.

Sincerely, Shannon

Response: See response to comment code 6120.

Commenter Name: Maureen Crossey
Commenter Organization: Packard Manse, Inc.
EPA Document ID: EPA-HQ-OW-2008-0692-1372
EPA Comment ID: 20397
EPA Comment Code: 6120

Comment: Regulate Perchlorate. We need to convince Americans to trust their water supply. Stop using bottled water and filling the land with plastic waste. Maureen

Response: See response to comment code 6120. Regarding commenter's statement about bottled water, the EPA does not have the authority to regulate bottled water and this statement is outside the scope of this regulatory action.

Commenter Name: J. Hammond
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1374
EPA Comment ID: 20398
EPA Comment Code: 6120

Comment: Please keep our drinking water safe -- the EPA needs to regulate perchlorate.

Response: Please see the umbrella response under 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1388
EPA Comment ID: 20399
EPA Comment Code: 6120

Comment: PLEASE NO ROCKET FUEL IN OUR DRINKING WATER.

I'M AN AMERICAN CONSUMER AND VERY CONCERNED ABOUT OUR DRINKING WATER AND ITS CONTAMINANTS. IT'S NO WONDER ALL OF US ARE PUTTING IN WATER PURIFIERS.

PLEASE PROTECT OUR WATER AND ELIMINATE ALL POISONS SO WE CAN DRINK PURE WATER.

Response: Please see the umbrella response under 6120.

Commenter Name: Julia Earl
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1389
EPA Comment ID: 20400
EPA Comment Code: 6120

Comment: As a children's environmental health advocate, I urge the EPA to keep perchlorate out of US drinking water supplies. This harmful chemical has no place in drinking water supplies. Special populations including pregnant women, infants, children and those of child-bearing age are particularly vulnerable. Therefore, I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Thank You, Julia Earl, MS

Response: See response to comment code 6120.

Commenter Name: Alisa Novelli
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1392
EPA Comment ID: 20401
EPA Comment Code: 6120

Comment: Please do not allow any amount of perchlorate in our drinking water It is a harmful chemical that can impair the thyroid gland which controls growth, development and metabolism.

Thank you, Alisa Novelli

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1397
EPA Comment ID: 20402
EPA Comment Code: 6120

Comment: NO Perchlorate in our drinking water!!!

Response: See response to comment code 6120.

Commenter Name: E. Granata
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1398
EPA Comment ID: 20403
EPA Comment Code: 6120

Comment: I urge you to reconsider your preliminary decision not to regulate the presence of perchlorate in drinking water. This is a public health hazard that can be remedied easily with standards set by EPA.

Response: See response to comment code 6120.

Commenter Name: L. Haas
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1399
EPA Comment ID: 20404
EPA Comment Code: 6120

Comment: Please reverse your decision regarding the regulation of perchlorate. It is the EPA's responsibility to regulate any and all substances in drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1401
EPA Comment ID: 20405
EPA Comment Code: 6120

Comment: please do not allow rocket fuels in our drinking water

Response: See response to comment code 6120.

Commenter Name: P. Leitzel
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1403
EPA Comment ID: 20406
EPA Comment Code: 6120

Comment: I have been informed that perchlorate is in rocket fuel and may soon be in our drinking water. What is with the EPA? You're here to protect the public, not poison us. Please do not deregulate the use of this substance. Thank you

Response: See response to comment code 6120.

Commenter Name: J. and M. V. Shaw Kline
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1406
EPA Comment ID: 20407
EPA Comment Code: 6120

Comment: Please reverse your decision not to regulate perchlorate in our drinking water. We are very short sighted when we do not protect our drinking water.

My vote is to regulate perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Mary Mintz
Commenter Organization: Northeast Organic Farming Association (NOFA)
EPA Document ID: EPA-HQ-OW-2008-0692-1407
EPA Comment ID: 20408
EPA Comment Code: 6120

Comment: It is obvious that we need to monitor as many pollutants as possible in our water supply for our health....need we say more?

Response: See response to comment code 6120.

Commenter Name: Mary Mintz

Commenter Organization: Northeast Organic Farming Association (NOFA)
EPA Document ID: EPA-HQ-OW-2008-0692-1408
EPA Comment ID: 20409
EPA Comment Code: 6120

Comment: Please consider reversing your decision to regulate perchlorate.....isn't this very toxic? Think future.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1410
EPA Comment ID: 20410
EPA Comment Code: 6120

Comment: Please reverse you decision on not regulating percholate in our water supply. There are so many destructive chemicals in our water now it is freightening. There is no reason to allow this harmful contaminate into the water supply. Allowing this chemical in our water supply will affect the health and safety of everyone. Please do the right thing for all of us. Regulate the admission of percholate now.

Response: See response to comment code 6120.

Commenter Name: Heather Morgan
Commenter Organization: Morgan Holistic Health
EPA Document ID: EPA-HQ-OW-2008-0692-1411
EPA Comment ID: 20411
EPA Comment Code: 6120

Comment: We,as health professionals, believe that Perchlorate needs to be removed completely from drinking water and water should be constantly monitored to insure no levels of this toxic chemical are detected. There is a health crisis in America, and part of this is due to environmental toxic exposure and we need to take action NOW to reverse the levels of exposure that are compiling from all forms of exposure which cause diseases in our bodies. Clean water, free of chemicals, is the most important thing we can do for our health.

Response: See response to comment code 6120.

Commenter Name: L. Huggins
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1416
EPA Comment ID: 20412
EPA Comment Code: 6120

Comment: Please, reconsider your decision, you MUST regulate perchlorate in drinking water as safety of population is extremely important for the future of the country and its resources.

Response: See response to comment code 6120.

Commenter Name: S. Kagen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1417
EPA Comment ID: 20414
EPA Comment Code: 6120

Comment: I protest this lackadaisical response to poison in our drinking water.

Here's an idea. Put a few drops of perchlorate into everything you drink, and everything you boil, like potatoes or broccoli. Wait two years and then get back to me on how your health is doing.

This will be overtuned in a heartbeat in a couple of months.

Do the right thing.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1420
EPA Comment ID: 20415
EPA Comment Code: 6120

Comment: Please regulate perchlorate so it cannot be added to our drinking water.

Response: Perchlorate is not added to drinking water. EPA has determined to regulate perchlorate, See response to comment code 6120.

Commenter Name: Melanie A. Marty, Ph.D.
Commenter Organization: Children's Health Protection Advisory Committee
EPA Document ID: EPA-HQ-OW-2008-0692-0962
EPA Comment ID: 20416
EPA Comment Code: 6120

Comment: November 3,2008 Stephen L. Johnson, Administrator United States Environmental Protection Agency 1200 Pennsylvania Avenue, N.W. Washington, D.C.. 20460 RE: Preliminary Regulatory Determination on Perchlorate; Docket ID No. EPA-HQ- OW-2008-0068

Dear Administrator Johnson:

The Children's Health Protection Advisory Committee (CHPAC) has been closely monitoring the Agency's approach towards perchlorate as a drinking water contaminant. Our March 2006 letter to you recommended that the Agency develop a federal Maximum Contaminant Level (MCL) for perchlorate. This recommendation was based upon the ability of perchlorate to disrupt thyroid hormone synthesis, lowering circulating levels of thyroid hormone, and the critical importance of thyroid hormone to brain development. Our concern over perchlorate has focused on in utero and

postnatal development, particularly for neonates whose exposures can be considerably greater than adults, and who lack stores of thyroid hormone. The life-long consequences of impaired brain development are sufficient to merit setting a protective MCL for perchlorate. Further, setting an MCL would mandate testing of public water supplies, and allow discovery of hot spots of contamination.

We are writing to you again on perchlorate because in the Preliminary Regulatory Determination on Perchlorate dated Oct 10, 2008, EPA decided against setting an MCL. This decision was based upon the establishment of a flawed benchmark, a Health Risk Limit (HRL) of 15 ug/L. This benchmark is clearly too high for infants as the Agency's own calculations show that an HRL of 15 ug/L would allow daily exposures to infants that are 2-5 times higher than the Reference Dose (RfD) (Federal Register, Vol 73, No.198, October 10, 2008, 60262-60282). The RfD is meant to be applied to everyone, yet in the case of perchlorate it is applied to adults but not infants. This decision does not recognize the science which supports the exquisite sensitivity of the developing brain to even small drops in thyroid hormone levels and the fact that neonates have much diminished stores of thyroid hormone relative to adults. The Agency must ensure that this life stage is adequately protected.

Response: See response to comment code 6120.

Commenter Name: Melanie A. Marty, Ph.D.
Commenter Organization: Children's Health Protection Advisory Committee
EPA Document ID: EPA-HQ-OW-2008-0692-0962
EPA Comment ID: 20424
EPA Comment Code: 6120

Comment: In summary, the CHPAC believes that all three conditions for setting an MCL are met and that the Agency must set an MCL for perchlorate. We request further communication with you and your staff regarding the Preliminary Regulatory Determination on Perchlorate. This is a critical and timely issue given the concerns over endocrine disruption by thyroid-active agents of various types and their potential to interact with other neurotoxicants to impair early life brain development. While many of these other neurotoxicants (heavy metals, pesticides, PCBs) have been aggressively targeted by USEPA, the lack of regulation of perchlorate is an obvious oversight that can readily be addressed. Thank you for your attention to this matter.

Sincerely, Melanie A. Marty, Ph.D., Chair Children's Health Protection Advisory Committee

Cc: Benjamin Grumbles, Assistant Administartor, OW Cynthia Dougherty, Director, OGWDW
Eric Burneson, Chief, Targeting and Analysis Branch, OGWDW

References:

Blount BC, Pirkle IL, Osterlob JD, Valentin-Blasini L, Caldwell K.L. 2006. Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environ Health Perspect 114:1865-1871.

Greer MA, Goodman G, Piens RC, Greer SE (2002) Health effects assessment for environmental perchlorate contamination: the dose response for inhibition of thyroidal radioiodine uptake in humans. Environ Health Perspect 110:927-937.

MADEP, 2006 Perchlorate Monitoring Results - Confirmed Above 1.0 ppb (Available at http://www.mass.govidep/water/drinlcing/percinfo.htm)

Response: See response to comment code 6120.

Commenter Name: Wenonah Hauter
Commenter Organization: Food & Water Watch
EPA Document ID: EPA-HQ-OW-2008-0692-1259
EPA Comment ID: 20425
EPA Comment Code: 6120

Comment: November 7, 2008

Water Docket Environmental Protection Agency 1200 Pennsylvania Ave., NW Washington, DC 20460

RE: Docket ID No. EPA-HQ-OW-2008-0692

Food & Water Watch, a Washington DC-based consumer advocacy organization, opposes the Environmental Protection Agency's Preliminary Regulatory Determination on Perchlorate.

Food & Water Watch hopes that the EPA will reconsider this preliminary determination and will issue a national primary drinking water regulation for perchlorate in accordance with the Safe Drinking Water Act.

Perchlorate has been found in the drinking water supply of 35 states and the District of Columbia. Widespread human exposure to perchlorate was confirmed by the Centers for Disease Control's NHANES study, which found that 100 percent of the 2,820 randomly selected study participants had detectable levels or perchlorate in their urine.[FNi: Blount, Benjamin C et al. "Perchlorate Exposure of the US Population, 2001-2002." Journal of Exposure Science and Environmental Epidemiology. 17: 400-407, 2007.]

The widespread exposure of the population to some level of perchlorate raises serious health concerns. Perchlorate can inhibit the thyroid gland's iodine uptake, potentially leading to hypothyroidism. Severe hypothyroidism during pregnancy can lead to abnormal fetal cognitive development, and even mild hypothyroidism during pregnancy is associated with subtle cognitive defects in children. Thus, perchlorate could alter fetal brain development, having lifelong cognitive effects for those affected.

The EPA's failure to regulate perchlorate in drinking water act places consumers - especially pregnant woman and children - at risk.

In response to this misguided determination, the EPA's own Children's Health Protection Advisory Committee has drafted a letter expressing its concern with the EPA's decision not to regulate perchlorate. Members of the committee claim that EPA rushed a decision on perchlorate without taking time to review all the latest peer-reviewed studies.

Given the vital importance of fetal central nervous development not only for long-term health and development of children, but also for the viability of fetuses, why would the EPA rush to a decision? Unfortunately the only conclusion we can draw is that the EPA has issued this determination to avoid strapping the Department of Defense with costs to clean-up near military bases, missile testing sites and chemical plants. While millions of consumers' health is jeopardized, it seems the budget concerns of the Pentagon or White House are driving EPA's decision.

This determination is clearly another instance of a regulatory agency shrinking from its responsibility to protect the American public. Instead of fulfilling your obligations under the SDWA, the EPA has once again folded to pressure.

Sincerely,

Wenonah Hauter Executive Director

Response: Please see response to comment code 6120.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection
EPA Document ID: EPA-HQ-OW-2008-0692-1422
EPA Comment ID: 20430
EPA Comment Code: 6120

Comment: November 6, 2008

Water Docket U.S. Environmental Protection Agency Mailcode 2822T 1200 Pennsylvania Avenue, NW Washington, D.C. 20460

Docket ID No. EPA-HQ-OW-2008-0692. Drinking Water: Preliminary Regulatory Determination on Perchlorate

The Massachusetts Department of Environmental Protection (MassDEP) is submitting the following comments in response to the United States Environmental Protection Agency's (EPA's) request for comment on its preliminary determination not to regulate perchlorate in drinking water at a national level, Docket ID No. EPA- HQ-OW-2008-0692 entitled "Drinking Water: Preliminary Regulatory Determination on Perchlorate". These comments were prepared by scientists in the MassDEP Office of Research and Standards (ORS) including Carol Rowan West, MPH, Director, ORS; Tsedash Zewdie Ph.D., Senior Toxicologist, ORS; and C. Mark Smith Ph.D., S.M., Deputy Director, ORS.

1. A Health Protective National Standard is Needed. MassDEP disagrees with EPA's draft decision not to regulate perchlorate at the national level and believes that a health protective national drinking water standard for perchlorate is both warranted and necessary to protect the health of our nation's children. Overall, EPA's assessment does not adequately support its determination to not regulate perchlorate for a sizeable number of United State' citizens, by disregarding elevated exposures and potential developmental effects in the neonate. This decision is inconsistent with basic precepts of public health protection.

Response: See response to comment code 6120.

Commenter Name: Carol Rowan West
Commenter Organization: Massachusetts Department of Environmental Protection
EPA Document ID: EPA-HQ-OW-2008-0692-1422
EPA Comment ID: 20436
EPA Comment Code: 6120

Comment: In conclusion, EPA's determination that a national drinking water is not warranted is based on an incomplete assessment of the data and will place many of the nation's most vulnerable citizens, our newborn children and fetuses at an early stage of development, at risk. MassDEP believes that there is compelling evidence to support a national drinking water standard for perchlorate at a value well below EPA's HRL of 15 ppb.

For further information please contact Carol Rowan West at 617-292-5510 (Carol.RowanWest@state.ma.us) or C. Mark Smith at 617-292-5509 (C.Mark.Smith@state.ma.us).

References

Blount BC, Pirkle JL, Osterloh JD, Valentin-Blasini L, Caldwell KL (2006). Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. Environ Health Perspect 114:1865-1871.

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Isaacs GH, Athans, JC, Rosenberg IN (1966). Effects of thyrotropin upon thyroidal iodide. Studies using thyroid venous cannulation and two radioiodine isotops. J Clin Invest 45:758

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Zoeller RT, Rice DC (2004). Critical effect of perchlorate on neonates is iodide l Pharmacol 40:376-377; author reply 378-379.

Response: See response to comment code 6120.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Dept. of Environmental Protection
EPA Document ID: EPA-HQ-OW-2008-0692-1526
EPA Comment ID: 20447
EPA Comment Code: 6120

Comment: November 10, 2008

Water Docket Environmental Protection Agency Mail Code: 2822T 1200 Pennsylvania Ave, NW Washington, DC 20460 RE: Docket ID No. EPA-HQ-OW-2008-0068

To Whom It May Concern:

Thank you for the opportunity to provide comments on the Preliminary Regulatory Determination on Perchlorate in Drinking Water proposed by USEPA, which was published in the Federal Register of October 10, 2008 (73 Fed. Reg. 60262-82 (October 10, 2008)). On October 7, 2005 the New Jersey Department of Environmental Protection (NJDEP) received from the New Jersey Drinking Water Quality Institute (NJDWQI), a legislatively created public advisory body, a recommendation to establish an MCL for perchlorate of 5 ug/L. The Department plans to propose such an MCL including monitoring and compliance determination requirements before the end of 2008 with adoption later in 2009. The NJDEP believes that having an MCL for perchlorate is good public health policy for both New Jersey and for the country as a whole.

There are two aspects of the proposal on which we would like to
Comment: 1) the proposal of a health reference level (hrl) for perchlorate of 15 ug/l. It is our understanding that an hrl is a drinking water concentration intended to protect individuals, including sensitive subgroups, from adverse effects resulting from a lifetime of exposure, similar to a lifetime health advisory or a maximum contaminant level goal. 2) The decision not to develop a regulatory standard (mcl) for perchlorate, and to develop guidance (a health advisory) instead, based on population exposed above the hrl.

Response: This is not a comment, a response is not necessary.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Dept. of Environmental Protection
EPA Document ID: EPA-HQ-OW-2008-0692-1526
EPA Comment ID: 20452
EPA Comment Code: 6120

Comment: Based on the above comments, we strongly urge USEPA to reconsider its conclusion that 15 ug/L is a health protective concentration for perchlorate in drinking water. We also strongly urge USEPA to reconsider its determination to not regulate perchlorate. The New Jersey Drinking Water Quality Institute recommendations regarding perchlorate can be found at http://www.nj.gov/dep/watersupply/perchlorate_mcl_10_7_05.pdf. For further information or clarification about our position, contact Dr. Eileen Murphy at 609-984-6070, or Eileen.murphy@dep.state.nj.us .

Sincerely,

Jeanne Herb, Director, Office of Policy and Planning

C: Michele Putnam, NJDEP Eileen Murphy, NJDEP Barker Hamill, NJDEP Sandra Krietzman, NJDEP Betty Boros-Russo, NJDEP Gloria Post, NJDEP Perry Cohn, NJDHHS Mark Robson, Chair, New Jersey Drinking Water Quality Institute

Citations

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Van den Hove, M.F., et al. (1999). Hormone synthesis and storage in the thyroid of human preterm and term newborns: effect of thyroxine treatment. Biochimie 81:563-570.

Zoeller, R.T. and Rice, D.C. (2004). Critical effect of perchlorate on neonates is iodide uptake inhibition (Letter to the editor). Regulatory Toxicology and Pharmacology, 40(3): 376-377.

Response: EPA has determined to regulate, See response to comment code 6120. Once the National Primary Drinking Water Regulation is final, EPA will consider revisions to the health advisory.

Commenter Name: Gregg Grunenfelder
Commenter Organization: Washington State Department of Health; and Oregon Department of Human Services
EPA Document ID: EPA-HQ-OW-2008-0692-1529
EPA Comment ID: 20453
EPA Comment Code: 6120

Comment: November 10, 2008

Docket ID No. EPA-HQ-OW-2008-0692

Water Docket Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Avenue, Northwest Washington, DC 20460

To Whom It May Concern:

Recently, the US Environmental Protection Agency (EPA) solicited comments for an action notice placed on the Federal Register relating to a preliminary regulatory determination for perchlorate in drinking water. The agency stated that levels of perchlorate found in drinking water systems were not at levels of concern and that there was no meaningful opportunity for health risk reduction through a national drinking water regulation. The Washington State Department of Health and the Oregon Department of Human Services disagree with EPA's conclusion and recommend that EPA reconsider the need for a national drinking water standard for perchlorate.

Extensive use and improper disposal of this highly water-soluble compound has led to groundwater contamination throughout the United States. To date, the extent of groundwater contamination has not been well characterized. It is known, however, that here in the northwest low levels of perchlorate have been found in groundwater in some tested areas of eastern Washington and Oregon.

Response: See response to comment code 6120. Regarding commenter's statement "…Extensive use and improper disposal of this highly water-soluble compound has led to groundwater

contamination throughout the United States", proper disposal of perchlorate is required by EPA's RCRA regulations and this subject matter falls outside of the scope of this regulatory action.

Commenter Name: James Barton
Commenter Organization: Underwater Ordnance Recovery
EPA Document ID: EPA-HQ-OW-2008-0692-1531
EPA Comment ID: 20460
EPA Comment Code: 6120

Comment: Opposition to EPA's Decision to Not Regulate Perchlorate - A Threat to the Great Lakes

James Barton, President - Underwater Ordnance Recovery jamesbarton@uwuxo.com Steve Pollack ESQ, - Director Blue Eco Legal Council steve@ecoesq.com

Removal of an estimated one million tons of unexploded ordnance and bulk containers abandoned on the floor of the Great Lakes is unlikely if the US EPA decision to deregulate perchlorates stands. Perchlorates are the most persistent munitions constituent leaching from decaying military explosives abandoned in a marine environment. Already beginning to show up at certain lakefront municipal water treatment facilities on both the US and Canadian sides, deregulation of perchlorates threatens the essential rational for removal of these "point source" emitters of perchlorates, and sets the stage for irreversible and unnecessary perchlorate contamination of the Great Lakes.

Rocket fuel is commonly provided as the most likely source for perchlorate contaminated drinking water. While perchlorates are used for that purpose, they are also a major component of conventional military explosives. Prior to WWII, Germany manufactured an entire class of civilian explosives based solely on perchlorates, and throughout WWII Russia manufactured numerous types of explosive filled projectiles containing up to 89% perchlorates by volume. The percent by volume of perchlorates used in period manufacture of US military explosives vary but 25% is a conservative number overall.

Unaware of the impending threat to the United States and Canadaâ€™s shared strategic asset known as the Great Lakes, the US Environmental Protection Agency is said to have bowed to pressure from the Pentagon, according to US Senate Environmental Committee Chair, Senator Barbara Boxer (D-CA), adding; "To see the Bush EPA just walk away is shocking". Paul Yaroschak, Pentagon Deputy Director for Emerging Contaminants denies this, saying; "We have not intervened in any way", adding "The EPA decision was based on the Safe Drinking Water Act".

The EPA has identified over 400 land based active or formerly used defense sites across 35 states where perchlorates have already been detected at dangerous levels in local aquifers, affecting an untold number of adjacent communities. Most of these sites have had little exposure to rocket fuel, but do have a documented history of military high explosive use or manufacture. Soils contaminated with decadeâ€™s worth of perchlorate laden high explosive residues have become "non- point" sources of pollution, and are as difficult and costly to remediate as the aquifers they continue to pollute every time it rains. By contrast, unexploded munitions and other defense wastes intentionally dumped and abandoned on the floor of the Great Lakes remain largely intact due to cold fresh waters, and fit the classic description of "point source" emitters of pollutants that can and must be eliminated.

The most common critical pathway for perchlorate to enter the human body is through contaminated drinking water. It primarily attacks the thyroid gland where it slows metabolic rate, which is why it was once used to fatten livestock and poultry before being linked to breast and testicular cancer. The thyroid glands of children are most susceptible to perchlorates, which can also be transferred to the fetus maternally. Women are said to be ten times more susceptible to perchlorate uptake than men.

The incredible persistence of perchlorate gives it the ability to migrate far from its point of origin, including into crops. Because of this persistence, the technical and economic challenges involved in attempting to eliminate perchlorate once it has entered an ecosystem illustrate that removal of point sources is the most economical course of action. Much of southern California for instance, is already forced to use perchlorate laced waters from the Colorado River, contaminated from a single DoD managed perchlorate manufacturing facility that used unlined retention ponds and operated in the middle of the Nevada desert; miles away from the Colorado River.

Some might be surprised to learn the scope of the problem in the Great Lakes, and canâ€™t imagine how or why it happened. The question is what we are going to do about it. Ask a Great Lakes resident and the answer is a foregone conclusion; pull the munitions and related defense wastes out of the Lakes before itâ€™s too late. While few are aware that high explosive filled munitions provide a substantial source of perchlorates, large numbers of munitions found elsewhere in a more advanced state of decay have been linked to a decline in fisheries. Where others were helpless to address such problems due to a lack of removal technology, we are not; but in fact are on the verge of choosing a similar fate.

The prime directive of the US Department of Defense is defending this nation against international strategic threats, and the projection of US influence and power; not long term domestic environmental threats, especially the ones they had a hand in creating. Allowing any waste originator into the decision making process regarding toxic waste clean up is a foolâ€™s game; and the DoDâ€™s dismal track record pertaining to underwater unexploded ordnance clean up bears this out. Where considerable resources are being devoted to protect the health and economic viability of individual communities from land based defense wastes that you can see; the health and economic viability of a nation is being neglected for what you canâ€™t.

Ask a US defense official what we are going to do about the defense wastes in the Great Lakes, and if you can get past the debate on whether the threat justifies remedial action, he will ask you who is going to pay for the clean up. At the upper levels in the Pentagon itâ€™s all about the money, and how long you can delay spending a dime on anything other than your prime directive. While that approach has worked well for them in the past, time is running out for the rest of us.

Deregulating perchlorate will not make it go away nor mitigate its harmful effects; using the Safe Drinking Water Act to justify it is an affront to our national identity; and its impact on the Great Lakes is a threat to our national security.

This action is clearly not the will of the men and women who proudly serve the US EPA, and does a disservice to the citizens whose interests they represent. Therefore, the decision to deregulate perchlorates must be delayed until after responsible leadership returns to the White House.

James Barton is an international expert on underwater ordnance, and regarded by some as the worlds leading expert on the subject.

Steve Pollack is the Director of Blue Eco Legal Council, specializing in environmental pollution at federal facilities.

Response: See response to comment code 6120. EPA acknowledges commenter's concern about the clean up of perchlorates in areas that serve as point source contamination to water, including The Great Lakes. The clean up of perchlorate contamination in the United States is related to EPA's CERCLA regulations and this subject matter falls outside of the scope of this regulatory action.

Commenter Name: J. Green
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0148
EPA Comment ID: 20461
EPA Comment Code: 6120

Comment: This is a Public Comment Regarding EPA's refusal to regulate Perchlorate under the Safe Water Drinking Act (Docket ID EPA-HQ-OW-2008-0692):

Perchlorate is a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children. Not regulating this harmful chemical in our drinking water is unacceptable.

Perchlorate is found in drinking water in 35 states, and according to the EPA's own data, 16 million Americans are at risk of being exposed to this dangerous chemical.

Response: See response to comment code 6120.

Commenter Name: J. Green
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0148
EPA Comment ID: 20463
EPA Comment Code: 6120

Comment: Native Americans and Hispanics are especially vulnerable in New Mexico, as we have so many military weapons production facilities here. Perchlorates way beyond allowable parts per billion have been found in groundwater and streams. It is unacceptable to sacrifice the health of people and the environment for the sake of military-industrial profit. The EPA is our only recourse for protection from being poisoned to death by our own government. Please do your job EPA and enforce our clean water laws. Thank you.

Response: See response to comment code 6120.

Commenter Name: Vicky and Bll Clary
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0622
EPA Comment ID: 20464

EPA Comment Code: 6120

Comment: Docket Identification (ID) Number: EPA-HQ-OW-2008-0692 Preliminary Regulatory Determination on Perchlorate Re: Request for extension of comment period

I am writing to express my concern regarding the EPA's failure to regulate perchlorate, as well as the proposed reference level, which fails to protect - and will adversely affect -- the health and development of hundreds of thousands, perhaps millions of American children.

If the dangers we even only restricted to 17 million people alone that would be enough to take a more serious look at regulating, but the numbers of people affected is more like 20 to 40 MILLION + ! Already synthyroid is the number two prescribed medication in the country. This a drain on the insurance companies not to mention the devistation thyroid desease causes the patient. This chemical has been shown to cause thyroid problems. As a thyroid patient I can tell you every day is a struggle to keep control of my symptoms and I would not wish it on any one especially our children!

Response: See response to comment code 6120.

Commenter Name: Eric Keller
Commenter Organization: Phi Alpha Delta, University of Detroit Mercy
EPA Document ID: EPA-HQ-OW-2008-0692-1428
EPA Comment ID: 20466
EPA Comment Code: 6120

Comment: The regulation of perchlorate in our nation's water ways is rationally needed. From our drinking water to storm drains; streams into lakes; swamps to our forests; our land to our produce; into our wildlife and livestock, even our families, friends, and children, this regulation is needed. Our constitution demands this of us, and we must not be divided in makiong this stand; for our states, for our nation.

The People, their representives, the courts, the administration, they all have a ligitimate use of authority to provide for and protect ourselves. It would be an unjustice to the american people in allowing this pollutent to contaiminate our nation, in this way, and amount, any longer. Half-measures have to be stopped. We must take a firm stand, here and now, to show the american people, individuals and businesses, government and religion, neighbors and strangers, freinds and fowes, all over the world that the american government, its agencies, like the Environmental Protection Agency, are not going to stand idely by, and watch pollutants or contaiminates distroy our environment and severilly harm human beings and other inhabitants of this planet. We are reasonable,rationial, understanding, and forgiving, but we can not afford to be ignorant or blind, we can not afford to be walked over and abused any more, no matter in what situation, isuues, or relm.

Please take a stand, and strictly,within reasoning and speed, regulate perchlorate, (and other contaiminates and/or pollutants like) it is our duty to our posterity.

Thank you for your time, consideration, and civil service,

Respectfully,

Eric Keller Vice President, Phi Alpha Delta University of Detroit Mercy
kelleree@students.udmercy.edu

Response: See response to comment code 6120.

Commenter Name: P. Pasles
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1431
EPA Comment ID: 20467
EPA Comment Code: 6120

Comment: I am writing to ask the EPA to reverse its preliminary decision that it will not regulate perchlorate in drinking water. I am the father of two small children, and I also have some professional training that allows me to understand the health issues (which have been established with the aid of statistical analysis-- I am a mathematician). Even a small amount of perchlorate can affect growth, and can cause other long-term health problems as well. It is prevalent in our water supply all over this country, and the EPA needs to show leadership on this issue so that standards are set at a national level.

Response: See response to comment code 6120.

Commenter Name: T. Novak
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1433
EPA Comment ID: 20468
EPA Comment Code: 6120

Comment: Just DO THE RIGHT THING!!!!!! Why in the world would you ever allow ANY rocket fuel into our drinking supply?

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1435
EPA Comment ID: 20469
EPA Comment Code: 6120

Comment: "I understand the dangers of perchlorate and ask you to keep the testing requirement intact for our public drinking water supplies. Removal of the testing requirement would eliminate detection of perchlorate in the case of accidental or intentional contamination of drinking water supplies, such as the Tewksbury Massachusetts contamination in 2004." . As a parent of 3 children, I feel it is vital to continue monitoring for this, and other contaminents. Thank you

Response: This regulatory action does not affect testing requirements for perchlorate in local jurisdictions. See response to comment code 6120.

Commenter Name: D. Waggoner

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1440
EPA Comment ID: 20470
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: M. Sonnenblick
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1441
EPA Comment ID: 20471
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills. As a public school educator we are seeing more and more children with educational deficits, including learning disabilities, autism/Asperger's disorders, speech and language needs, and occupational therapy issues. These are expensive to remediate and often cause life-long struggles for the children and their families. We need to decrease the risk of babies developing these problems. Please regulate perchlorate and all other risky chemicals found in drinking water supplies.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1444
EPA Comment ID: 20472
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

As a registered nurse and a mother, I am concerned about the effects of low levels of perchlorate contamination on human thyroid function, and the consequent harm to developing fetuses, infants and children.

Response: See response to comment code 6120.

Commenter Name: G. Bastien
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1446
EPA Comment ID: 20473

EPA Comment Code: 6120

Comment: Perchlorate should not be used in drinking water because of the threat to endocrine system. thyroid disruption is not something to be trifled with because of it overall impact on mood, general health, etc.. Mammalian studies have sent out warnings to public health officials giving us a choice to use greater filtration in better water treatment plants while we clean up our ground and surface water.

I urge the EPA director to reverse the decision to allow the use of perchlorate in our water treatment plants.

Sincerely,

Greg Bastien 2709 E. Minnehaha Parkway Minneapolis, MN 55417

Response: See response to comment code 6120.

Commenter Name: Tom
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1450
EPA Comment ID: 20474
EPA Comment Code: 6120

Comment: Please regulate and limit Perchlorate emissions.

Perchlorate has been shown to damage the thyroid at very low concentrations, which in turn can lead to developmental problems, particularly in children.

Thank you. Tom

Response: See response to comment code 6120.

Commenter Name: M. J. Strawn
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1451
EPA Comment ID: 20475
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Perchlorate contamination is a nationwide problem which has health impacts at lower levels than previously thought.

EPA agrees that perchlorate has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people -- and other estimates of human perchlorate exposure are higher.

Even in small amounts, perchlorate can impair the thyroid gland, which controls growth, development, and metabolism. Developing fetuses, infants, and children with thyroid impairment may suffer mental retardation, loss of hearing and/or speech, or deficits in motor skills.

Exposure via drinking water occurs constantly, every day, for extremely long periods of time. EPA should not shirk its responsibilities to ensure the safety of twenty million people via this route.

Please regulate the amount of perchlorate in drinking water. Twenty million Americans are counting on you.

Response: See response to comment code 6120.

Commenter Name: J. Hudson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1454
EPA Comment ID: 20476
EPA Comment Code: 6120

Comment: I am concerned about the decision not to regulate perchlorate in our drinking water. Since this agent is so widespread in our country-found in 37 states-it seems even more critical to both regulate and monitor its effect on such a huge segment of the population.

I hope the EPA will reconsider this decision for the health of all, but especially the very young and the unborn.

Thank You

Jim Hudson

Response: See response to comment code 6120.

Commenter Name: M. Nolasco
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1464
EPA Comment ID: 20477
EPA Comment Code: 6120

Comment: I am writing to urge the US EPA to reverse its determination not to set a regulation for perchlorate in drinking water.

The health impact of percholate contamination is a nationwide problem.

Please keep this out of our drinking water.

M. Nolasco

Response: See response to comment code 6120.

Commenter Name: T. Bell
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1465
EPA Comment ID: 20478
EPA Comment Code: 6120

Comment: I am very concerned that we, as a country, are not doing more to insure clean and safe water standards. More and more compounds in our water have been found to have adverse effects in extremely small amounts that are currently legal. To relax or expand allowable amounts of trace poisons that hurt our children and county is just not right.

Response: See response to comment code 6120.

Commenter Name: Leslie McCollom
Commenter Organization: O'Hanlon, McCollom & Demerath
EPA Document ID: EPA-HQ-OW-2008-0692-1467
EPA Comment ID: 20479
EPA Comment Code: 6120

Comment: My name is Leslie McCollom, and I am a private individual who practises law in Austin, Texas, at 808 West Avenue, Austin, Texas 78701. I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. The reasons for my objections to your agency's preliminary determination is because perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought, according to research I have reviewed. I see no need to list all of the sources, since I am assuming that your agency has done its homework and reviewed all available data, research, and opinion on the effects of this chemical. A national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Perchlorate is a harmful chemical used in rocket fuel, flares, and explosives. Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills as a result of consuming this chemical It is my understanding that the EPA agrees that perchlorate has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher. Under these circumstances, I believe the EPA has a legal duty to set a standard for this harmful chemical in drinking water, as well as in any and all bodies of water that are subject to regulation under the Clean Water Act.

Leslie McCollom O'Hanlon, McCollom & Demerath 808 West Avenue Austin, Texas 78701 (512) 494-9949

Response: See response to comment code 6120.

Commenter Name: SueAnn Hurley
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1459
EPA Comment ID: 20480

EPA Comment Code: 6120

Comment: To Whom it may concern: I urge the EPA to reverse your recent decision not to regulate perchlorate in public drinking water. It is too risky and dangerous. Thank you, SueAnn Hurley

Response: See response to comment code 6120.

Commenter Name: J. Egan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1455
EPA Comment ID: 20481
EPA Comment Code: 6120

Comment: Maintaining current standards for perchlorate content is needed to clean up existing ground water contamination and prevent future spills. Although the cost is significant, the degradation of our environment is more costly; in increased health care costs, loss of productivity, and land value.

Response: This is not a comment. No response necessary.

Commenter Name: Richard, Alison, Henry Whittaker
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1473
EPA Comment ID: 20482
EPA Comment Code: 6120

Comment: I am writing in support of maintaining high standards of water purity -- keeping perchlorate OUT of drinking water. Friends and family suffer from thyroid problems and perchlorate has been linked to thyroid problems. DO NOT RELAX any standards that would allow perchlorate in our drinking water. Richard, Alison & Henry Whittaker 103 Marin Street San Rafael CA 94901

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1474
EPA Comment ID: 20483
EPA Comment Code: 6120

Comment: PLEASE reconsider your position on Perchlorate. While the pharmaceutical companies may like things just the way they are, we have to protect the public, especially children. With all the endocrine and other health problems plagueing this country, we need to reduce the amount of toxins that go into our bodies.

Response: See response to comment code 6120.

Commenter Name: Ann Galbraith Miller
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1477
EPA Comment ID: 20484
EPA Comment Code: 6120

Comment: Good Day, I am writing to urge you to disallow perchlorate in drinking water sources because it can create more impacts on human health than previously recognized. Since it your mission to protect public health, it seems obvious that you would act now to pull back on the decision to allow "safe" levels of this dangerous threat. Thank you, Ann Galbraith Miller

Response: See response to comment code 6120.

Commenter Name: Susan Dunham
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1478
EPA Comment ID: 20485
EPA Comment Code: 6120

Comment: Please reconsider the consequences of not regulating perchlorate. Is this water you will be drinking? Is this water your family will be drinking? If it were, would you be making this decision knowing the harmful effects perchlorate can have on the health of the people who are exposed to it. We have had enough with the past administration looking the other way in other situations. Let's not continue down the same road. You are the individuals that Americans hold responsible for our health and well being. If we can't count on you to do your jobs who can we count on? By choosing to support national regulations on public drinking water we know we can continue to trust you with health related issues. Please reverse your decision.

Sincerely, Susan Dunham

Response: See response to comment code 6120.

Commenter Name: T. Bramwell
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1479
EPA Comment ID: 20486
EPA Comment Code: 6120

Comment: we need percholate testing in our water, and we need to move toward the banning of percholate that is enhanced by man-made action, or lack of action.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1480
EPA Comment ID: 20487
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: T. O'Brien
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1484
EPA Comment ID: 20488
EPA Comment Code: 6120

Comment: All possible steps need to be taken to eliminate or reduce to safe levels all contaminants in our drinking water. You need to protect our health.

Response: See response to comment code 6120.

Commenter Name: Molly P.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1486
EPA Comment ID: 20489
EPA Comment Code: 6120

Comment: To the U.S. Environmental Protection Agency: I am a normal 30 year old professional woman from MN and was shocked and disgusted to learn about the EPA decided to not regulate perchlorate in drinking water. Please reverse your preliminary determination on setting a regulation for perchlorate in drinking water! It should be the goal of the EPA to protect the health and welfare of Americans, not to gamble with our future by allowing the contamination of our nation's water supply! In Minnesota we are now seeing the consequences of poor decisions like the one you are about to make. In many lakes and rivers it is no longer save to catch and eat fish, some waters are even unswimable. Consider the quality of limited resources you will be leaving for children and grandchildren. Do not take chances with something as critically important as keeping our nation's drinking water clean!! Thank you for your consideration, Molly P.,Minneapolis, MN

Perchlorate FACTS: Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought;

a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Perchlorate is a harmful chemical used in rocket fuel, flares, and explosives.

Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism.

Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

EPA agrees that perchlorate has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1490
EPA Comment ID: 20490
EPA Comment Code: 6120

Comment: It is a generally acknowledged fact that our planet is suffering from the dangerous effects of human industrialization, most publicly understood as global warming. More and more people are working to become responsible stewards of the earth by consuming less, buying organic and recycling; all the while an insidious danger flows quietly beneath our feet.

Perchlorate is an environmental danger widely known amongst scientific communities and government agencies, yet virtually unheard by the public. So much research has been done on the existence of perchlorate contamination in our water, food and milk supplies, and yet nothing is being done to regulate it. Much worse than a passive lack of action, is the very active suppression by certain U.S. agencies to protect their very specific interests, at the great expense to our country's environment and the health of those who inhabit it.

The EPA's website is full of information on how to contribute to the health of the environment from our classrooms to our beaches, from "purchasing green" to reducing water waste. It's wonderful to see the EPA helping people to make a positive impact on an individual level.

Isn't it time for the EPA to take a responsible stand and make the decision to regulate perchlorate in drinking water? Please, help protect the health of our people, ecosystems and future. Without water, we are nothing.

Thank you.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1492
EPA Comment ID: 20491
EPA Comment Code: 6120

Comment: As someone who now suffers from thyroid dysfunction after many years of normal thyroid function, I urge the EPA to reconsider their decision to allow perchlorate contamination in our drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1494
EPA Comment ID: 20492
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

1. As a consumer, I depend on the EPA to protect my health. 2. Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; 3. Since even small amounts can impair development and metabolism, the EPA should err on the side of caution and keep perchlorate out of the water supply.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1495
EPA Comment ID: 20493
EPA Comment Code: 6120

Comment: If we cannot be assured of CLEAN drinking water because of a lax EPA, this country is in serious trouble!

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1500
EPA Comment ID: 20494
EPA Comment Code: 6120

Comment: All pollutants and contaminants to drinking water must be monitored and reported. Public interest demands this to protect the health of the public. Transparency is essential to good governance and to democracy itself. Perchlorate is in no way naturally found in water and is harmful to human health. The EPA must not lower standards. Its responsibility is to the public and not to particular industrial or corporate interests.

Response: See response to comment code 6120.

Commenter Name: R Cooper Jr.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1501
EPA Comment ID: 20495
EPA Comment Code: 6120

Comment: Any foreign substance in our drinking water is serious and is not acceptable. "Perchlorate," a jet fuel additive, is pure negligence to be tolerated in public drinking water that is

consumed and used for cooking and bathing purposes by innocent families and their children. We don't need deliberate health threats to our population to add to their already stressed state of health. Please consider the consequences and act on improving actions on this social issue. Every man, woman, and child is involved in this life threatening situation.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1502
EPA Comment ID: 20496
EPA Comment Code: 6120

Comment: I am dismayed at the EPA's preliminary decision not to regulate perchlorate in drinking water. Perchlorate has been shown to inhibit proper function of the thyroid. As the father of a young son, and another child on the way, I am extremely concerned about dangerous chemicals present in our drinking water. Even a small reduction in thyroid function results in a loss of IQ, and increased behavioral problems. The EPA was on a sensible course to limit exposure to this dangerous chemical around 2002. I am appalled that the safety of our children is being ignored due to political considerations. I have been extremely upset at the course the EPA has taken over the last 8 years, allowing the White House and politics to sway decisions that should be made based on science and for the health and safety of the American people.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1504
EPA Comment ID: 20497
EPA Comment Code: 6120

Comment: We need regulation of perchlorate in our drinking water.

Response: See response to comment code 6120.

Commenter Name: A.M. Guckin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1506
EPA Comment ID: 20498
EPA Comment Code: 6120

Comment: I am very concerned about the safety of US public water drinking water supplies. Keep the perchlorate out of the water. Test for it.

When contaminants are found, everyone in the region that uses that source for their household water needs to be informed and advised how to avoid consumption of the contaminants. We do not want to be forced to buy bottled drinking water - especially when we don't know what level of contaminants are permitted in the bottled water supply.

Thank you for your attention and please do all possible to insure that we have clean, safe drinking water.

Response: This regulatory action does not affect testing requirements for perchlorate in local jurisdictions. Please See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1507
EPA Comment ID: 20499
EPA Comment Code: 6120

Comment: I am asking the Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. We need to PROTECT OUR EARTH BECAUSE IT IS WHAT IS PROTECTING US. If we continue to violate and contaminate and pollute our earth, WE are the ones who suffer now and will suffer even more, until we make ourselves and other species totally extinct.

Response: See response to comment code 6120.

Commenter Name: D. Smythe
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1509
EPA Comment ID: 20500
EPA Comment Code: 6120

Comment: The determination of whether to control the level of perchlorate contaminates in drinking water supplies by the EPA has taken at least six years. Drinking water, groundwater or soil in hundreds of locations in at least 43 states is polluted with perchlorates. In 2004, eight states had advisories for perchlorate in drinking water, ranging from 1 to 18 parts per billion. Given the geographical magnitude of the problem and the diversity of current regulation, it is imperative that we have a Federal standard to protect everyone in the United States equally.

That standard should recognize the scientific study that has gone on to determine a safe level, and should not be politicized or modified to suit defense contractors.

Please set a standard of no more than 2 parts per billion.

Response: See response to comment code 6120.

Commenter Name: L. Brooks
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1512
EPA Comment ID: 20501
EPA Comment Code: 6120

Comment: Please make testing mandatory for Perchlorate in out drinking water. We need to be vigilent in maintaining our most valuable resources of fresh water vital to the good health of the general public.

Response: This regulatory action does not affect testing requirements for perchlorate in local jurisdictions. Please see response to comment code 6120.

Commenter Name: Nancy Stefanou
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1514
EPA Comment ID: 20503
EPA Comment Code: 6120

Comment: As a citizen, I ask you to remember your responsibilities to 'protect' (as in the Agency name) public interests. The umbilical cords of newborns are already showing the presence of an alarming number of chemicals...preventing exposure is vastly preferable to damage control. Again, please remember who you serve.

Thank you, Nancy Stefanou 2582 Black Pine Trail Troy, Mi 48098

Response: This is not a comment, a response is not necessary.

Commenter Name: Lesley Cox
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1516
EPA Comment ID: 20505
EPA Comment Code: 6120

Comment: Perchlorate exposure recommended by National Academy of Sciences and adopted by EPA is an RfD of 0.7 µg/kg bw/day, this is daily exposure level over a lifetime that is not expected to cause adverse health effects. We already know perchlorate is in some public drinking water systems and in some foods. It makes no obvious sense to ignore it. We have methods to test for detection, why not use them? EPA is our regulatory agency for protecting our country's drinking water. Do your job!!!!

Lesley Cox Carrabelle, FL

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1517
EPA Comment ID: 20506
EPA Comment Code: 6120

Comment: As a resident of Tewksbury, MA and a journalist, I urge that the EPA require perchlorate testing of drinking water. I know the potential dangers of perchlorate to women and infants due to an corporate dumping of perchlorate into the Merrimack River in Massachusetts in

2004. That dumping went straight into Tewksbury's water supply, preventing residents from drinking the water for several weeks and costing the town a tremendous amount of money to locate the problem, stop the problem, and ensure the quality of the water. Testing public water supplies, particularly those drawn from rivers, ensures early detection of tainted water and early notification of at risk populations. Further, regular testing and early detection helps identify polluters early and stop the pollution. Not testing for perchlorate in the water supply is irresponsible from a public health and environmental perspective.

Response: This regulatory action does not affect testing requirements for perchlorate in local jurisdictions. Please see the response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1519
EPA Comment ID: 20507
EPA Comment Code: 6120

Comment: we do not want perchlorate in our drinking water. it is clear we need to punish those in the federal govt who are not taking steps to protect americans. i note that the dept of defense of our own govt is one of the worst polluters. those in charge at this agency should go to jail for their lifetimes for poisoning fellow americans. no perchlorate in our drinking water should be allowed.

Response: See response to comment code 6120.

Commenter Name: D.E. McKenney
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1524
EPA Comment ID: 20508
EPA Comment Code: 6120

Comment: In 2004, Tewksbury Massachusetts had a perchlorate contamination that prohibited the use of our tap water. I understand the dangers of perchlorate and ask you to keep the testing requirement intact for our public drinking water supplies. Removal of the testing requirement would eliminate detection of perchlorate in the case of accidental or intentional contamination of drinking water supplies thereby endangering us all.

Response: This regulatory action does not affect testing requirements for perchlorate in local jurisdictions. Please see the response to comment code 6120.

Commenter Name: Chris Christensen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1535
EPA Comment ID: 20509
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

* perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; * a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Perc is still used in a majority of clothes cleaners/laundries across the nation. I chose to switch cleaners as a result. It should not be part of our drinking water.

Chris Christensen 1160 N. Beverly Lane Arlington HTs, IL 60004

Response: See response to comment code 6120.

Commenter Name: Beatriz Bofill
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1536
EPA Comment ID: 20510
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought. A national primary drinking water regulation would provide a meaningful opportunity to protect public health.

If we do not learn from our past mistakes, we are doomed to repeat our failures over and over. Not protecting Americans from this contaminant will only cause greater problems further down the road.

Hopefully with the new administration, this will be a non issue and I won't have to waste my time writing about a no-brainer decision as to establish and enforce an MCL on perchlorate.

Sincerely, Beatriz Bofill

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1540
EPA Comment ID: 20511
EPA Comment Code: 6120

Comment: There are existing studies that prove exposures to perchlorate have adverse effects on a woman's thyroid. How can we allow this toxin into our drinking water when it is known to be harmful?

According to a 2006 study by researchers at the centers for disease control and prevention (cdc), it was concluded that american women, particularly those with low iodine intake, may have reduced thyroid function due to perchlorate exposure.

Please do not allow this harmful toxin to be unregulated when it comes to our drinking water.

Response: See the response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1541
EPA Comment ID: 20512
EPA Comment Code: 6120

Comment: There is sufficient evidence to warrant the regulation of perchlorate in drinking water. Please do so. Regards.

Response: See response to comment code 6120.

Commenter Name: Virginia Schulman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1542
EPA Comment ID: 20513
EPA Comment Code: 6120

Comment: I represent no organization, and no government agency at any level. I am a concerned citizen, parent, and grandparent, and what's more, I care about my own health as well. Perchlorate does not belong in our drinking water. It needs to be regulated. How many toxins have we allowed into our environment only to say, years later, "Oops! Now you have cancer. My bad!" We don't need to wait for years to say that perchlorate does not belong in our drinking water. We need to regulate it and keep it out of our water supplies. Doing nothing is not neutral; it's hostile to the people of the United States. In my book, that's treason. The EPA is supposed to protect us, not totally ignore our health on behalf of industry.

Virginia Schulman Northampton, Massachusetts

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1543
EPA Comment ID: 20514
EPA Comment Code: 6120

Comment: I agree that this substance should NOT be in our drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1545
EPA Comment ID: 20515

EPA Comment Code: 6120

Comment: Rocket fuel in our water supply is domestic terrorism!

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1546
EPA Comment ID: 20516
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

The side effects of even a minor amount of this contaminate in our water supply can have serious effects on children and pregnant mothers. Please DO NOT let this opportunity pass to set up safe and effective regulations for our citizens

Response: See response to comment code 6120.

Commenter Name: Aaron J. Skoglund
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1547
EPA Comment ID: 20517
EPA Comment Code: 6120

Comment: I am concerned about the allowance of dangerous chemicals like perchlorate in our drinking water. I think that everything possible should be done to keep our nation's drinking water pure and clean. I urge the EPA to reconsider its allowance of perchlorate in drinking water at any level. The citizens of this country need to know that our health and well being is the EPA's top priority. There should be next to no room for compromise on this principle.

Sincerely, Aaron Skoglund Amherst, MA

Response: See response to comment code 6120.

Commenter Name: Thomas L. Schoaf
Commenter Organization: Cities of Litchfield Park and Goodyear, AZ
EPA Document ID: EPA-HQ-OW-2008-0692-1552
EPA Comment ID: 20518
EPA Comment Code: 6120

Comment: November 5, 2008 Stephen L. Johnson, Administrator U.S. Environmental Protection Agency Ariel Rios Building 1200 Pennsylvania Avenue, N.W. Washington D.C . 20460 Re:Preliminary Regulatory Determination on Perchlorate Docket ID No . EPA-HQ-OW-2008-0068

Administrator Johnson:

We, the undersigned, represent the cities of Goodyear and Litchfield Park. Our communities are located in the West Salt River Valley area of metropolitan Phoenix in central Arizona and are impacted or threatened by the Phoenix- Goodyear Airport (PGA) North federal superfund site. The PGA North federal Superfund Site is an area of groundwater that has been impacted by TCE and perchlorate and it is this perchlorate contamination that prompts us to request that the EPA reconsider its determination and establish a national maximum contaminant level for perchlorate.

By way of background, surface water supplies in Arizona are limited and are fully allocated. Thus, groundwater is a vital water resource in the arid southwest providing a reliable future municipal supply for our growing communities. It is of such importance that Arizona classifies all aquifers as drinking water aquifers. Arizona, as with many other states, adopts the federal maximum contaminant levels (MCLs) as its own drinking water standards. Arizona also establishes aquifer water quality standards for the protection of its aquifers. Since Arizona's aquifers are classified as drinking water aquifers, the established aquifer water quality standards are generally equivalent to the MCLs.

Response: See response to comment code 6120.

Commenter Name: Richard Mead
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1553
EPA Comment ID: 20521
EPA Comment Code: 6120

Comment: The refusal of the EPA to regulate perchlorate in drinking water is an abrogation of the EPA's responsibilities.

Perchlorate is known to cause health problems to infants and adults that can be fatal or lead to permanent life-long disabilities.

Refusing to acknowledge this problem is tacit approval of those whose cause the pollution. The American tax payer is entitled to better protection than is currently provided, and should rightfully expect the EPA to manage this problem and hold the polluters accountable for cleaning up the problem and eliminating further contamination.

Richard Mead

Response: See response to comment code 6120.

Commenter Name: Crystal D. Lay
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1557
EPA Comment ID: 20522
EPA Comment Code: 6120

Comment: Comments submitted to Environmental Protection Agency regarding: Preliminary Regulatory Determination on Perchlorate in Drinking Water RIN 2040-ZA02

I respectfully request EPAâ€™s consideration of the following comment regarding RIN 2040-ZA02:

I would urge EPA to reconsider setting a maximum contaminant level for perchlorate in drinking water for several reasons:

1. Perchlorate can interfere with the functioning of the thyroid gland causing serious health effects, especially in developing children.

2. If not regulated, the daily perchlorate intake can easily exceed the RFD of 0.7 Âµg/kg.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1565
EPA Comment ID: 20524
EPA Comment Code: 6120

Comment: Please regulate perchlorate in drinking water. This is a public health issue. This chemical can cause thyroid problems affecting growth and development.

Response: See response to comment code 6120.

Commenter Name: C. Kennedy
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1569
EPA Comment ID: 20525
EPA Comment Code: 6120

Comment: I think that anything that is as harmfull as rocket fuel is to humans should be regulated in our drinking water no matter how many PPM are deemed acceptable. By not doing so there is a big loop hole where millions of americans are then subjected to something that they are unaware of and may cause serious health hazards. First - on a personal note my mother had Non Hodgekings Lymphoma. Our family is unsure of what may have caused this. We had a well and if our water was tested who knows what that test would find. Or for that matter when people are going through a healh crisis it is better to be sure nothing like this would be introduced or reintroduced in their system. Second- Is it not better to try and regulate now and not in the future when there may be reason to have a huge multi person lawsuits. Does anyone really want to drink any persent of rocket fuel, maybe you folks at the EPA do but I don't! Thank you for your attention to this matter.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1570
EPA Comment ID: 20526

EPA Comment Code: 6120

Comment: I urge the EPA to reverse it's decision re: perchlorate regulation. We now know that it has health impacts at lower levels than was previously recognized; with regulation public health could be protected. Thank you.

Response: See response to comment code 6120.

Commenter Name: Karen Cornelius
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1576
EPA Comment ID: 20527
EPA Comment Code: 6120

Comment: I am writing to urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. I think no doing so puts people's health at risk, even at low levels. It can impair the thyroid gland. This could be especially harmful to developing fetuses, infants and children with thyroid impairments. I heard it has been found in sites in 37 different states. This is way too many. (For me, anyone would be too many.) Please protect the health of vulnerable citizens. Thank you for your consideration. Karen Cornelius

Response: See response to comment code 6120.

Commenter Name: M. Maguire
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1577
EPA Comment ID: 20528
EPA Comment Code: 6120

Comment: Please protect the American public and keep perchlorate out of our drinking water. Thank you.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1579
EPA Comment ID: 20529
EPA Comment Code: 6120

Comment: There shouldn't be any perchlorate in our drinking water. Please reconsider the decision not to regulate this chemical.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-1582
EPA Comment ID: 20530
EPA Comment Code: 6120

Comment: Please regulate Perchlorate levels in our drinking water...We don't need any more potentially hazardous chemicals in our life sustaining water.

Response: See response to comment code 6120.

Commenter Name: Josephine Primeau
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1583
EPA Comment ID: 20531
EPA Comment Code: 6120

Comment: Please, no Perchlorate in our drinking water! The risks to the public health far outweigh any argument to allow it. Please keep the well-being of the citizenry of the United States your priority rather than acting out of convenience.

Respectfully, Josephine Primeau

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1585
EPA Comment ID: 20532
EPA Comment Code: 6120

Comment: I have heard that the EPA is considering the deregulation of perchlorate in our water systems. I do not know what to believe and cannot imagine that this is true. I know that many of us would like clarification. If this is true, I am against it. Thank you.

Response: On October 10, 2008 EPA published in the Federal Register a preliminary determination that a national primary drinking water rule was not necessary for perchlorate. However, EPA has now decided to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1587
EPA Comment ID: 20533
EPA Comment Code: 6120

Comment: Please do not deregulate PERCHLORATE in drinking water. We must protect our water and our environment. Isn't that the function of the EPA protect our land and water? Isn't that why we the people created the EPA? Companies are not good at policing themselves.Just do the job you are suppose to do! Please do not go in the same direction as the Federal Reserve did with the banking!!

Response: See response to comment code 6120.

Commenter Name: Amanda Forys-French
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1591
EPA Comment ID: 20534
EPA Comment Code: 6120

Comment: To Whom it Concerns: It is hard for me to believe that anyone in their right mind would allow a substance such as perchlorate to remain in our water. I urge you as a consumer of water to please regulate perchlorate for my sake, for the sake of my family and all of America. We have enough worries as to what may be in our food and water and this does not need to be another one. Please help! Thank you, Amanda Forys-French

Response: See response to comment code 6120.

Commenter Name: Robin M. Chambers
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1592
EPA Comment ID: 20535
EPA Comment Code: 6120

Comment: I am hoping that the new administration will take more interest in providing me an healthy enviroment . The EPA has not done anything for the last eight years to further this cause . I am one of very many who does not want Perchlorate in my drinking and more importantly in my childrens and grand childrens who will have have a long exposure to it .Please do what the agency was set up to do that is provide us with a safe enviroment . Thank you Robin M Chambers

Response: See response to comment code 6120.

Commenter Name: A. White
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1596
EPA Comment ID: 20536
EPA Comment Code: 6120

Comment: please keep us safe from harmful cemicals..

Response: This is not a comment, a response is not necessary.

Commenter Name: Jan Bourdelle
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1597
EPA Comment ID: 20537
EPA Comment Code: 6120

Comment: Hello, please do not allow perchlorate contamination in our water. I have thyroid issues as do many, many people. The medicine for it is a permanent life long commitment. As many of us cannot afford healthcare, it will cause that much more of a financial burden on our citizens to support their impaired thyroids due to this chemical's present in our drinking water. Thank you.

Jan Bourdelle, 458 Gail Dr., Nazareth PA 18064

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1598
EPA Comment ID: 20538
EPA Comment Code: 6120

Comment: no perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: B. A. Provost
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1603
EPA Comment ID: 20539
EPA Comment Code: 6120

Comment: Too many environmental protections have been lost in the last 10 or so years and we certainly can not afford to be further concerned about the safety of our drinking water. To allow something as hazardous to health as perchlorate in our water should call for anyone involved in EPA or the Bush administration orchestrating these criminal acts to be prosecuted in court. It is indeed a criminal act to allow an agent of death to be harbored in the water we must all have to survive. Governments have pursued the removal of trans-fats and nicotine from the public scene and turn around and let this go on. Such a travesty!

Response: This is not a comment, a response is not necessary.

Commenter Name: Van Landuyt
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1608
EPA Comment ID: 20540
EPA Comment Code: 6120

Comment: No to perchlorate in tap water. Need a citizen ask?

Response: See response to comment code 6120.

Commenter Name: Anonymouos
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1610

EPA Comment ID: 20541
EPA Comment Code: 6120

Comment: Every adult and child deserves to have clean drinking water. The health consequences of contaminants is not fully known so we need to be vigilant.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1612
EPA Comment ID: 20542
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Perchlorate causes too many harmful effects to humans in even small amounts. As a tax paying and contributing citizen of this country I have a right to safe drinking water. In the future, as I decide to have a family, I want my children to have access to safe drinking water, not water that could cause them to have birth defects or negative consequences to their health. Please don't allow perchlorate in our water. Thank you for your time.

Response: See response to comment code 6120.

Commenter Name: Elise Sullivan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1613
EPA Comment ID: 20543
EPA Comment Code: 6120

Comment: Please limit the amount of percholate allowed in our water. As a family physician, I am concerned about medical effects, such as affecting thyroid function by this chemical. Thank you, Elise Sullivan, M.D. Santa Rosa, CA

Response: See response to comment code 6120.

Commenter Name: S. L. Jackson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1614
EPA Comment ID: 20544
EPA Comment Code: 6120

Comment: I do NOT want perchlorate to be tolerated/ ignored in public drinking water supplies -- nor in water supplied to farms and animals.

For that matter, I don't want rocket fuel to be polluting the air I have to breathe, either, but I guess this battle against killer chemicals must be waged one painful step at a time. S.L. Jackson Randolph, NJ

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1617
EPA Comment ID: 20545
EPA Comment Code: 6120

Comment: To not monitor and regulate potentially toxic substances in drinking water endangers the well being of all organisms that ingest the substance. I urge the EPA to carry out its mandate protecting the health of the American People.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1618
EPA Comment ID: 20546
EPA Comment Code: 6120

Comment: Please regulate perchlorate in our drinking water!!! I'm very concerned with the pollutants found increasingly in our drinking water. Drugs, MTBE, perchlorate, pesticides.....how are our children going to survive all this? Are these chemicals harming our children, do we even know? Isn't it true that even in small amounts perchlorate can cause thyroid impairment? Please do everything you can to provide this country with safe water to drink.

Response: The statement regarding drugs, MTBE, and pesticides fall outside the scope of this regulatory action. Regarding the remainder of the comment, please see the response to comment code 6120.

Commenter Name: Denise F. Sipple
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1621
EPA Comment ID: 20547
EPA Comment Code: 6120

Comment: To: Stephen L. Johnson, Administrator, EPA From: Denise F. Sipple, Rumson, NJ Re: Enforceable limits for perchlorate in our drinking water

I recently lost my only child to cancer. Please protect the health of millions of American families and set enforceable limits for perchlorate in our drinking water. Specifically, I am writing to urge you reverse EPA's preliminary regulatory determination and set a protective drinking water standard for perchlorate as required by the Safe Drinking Water Act.

Perchlorate contamination in our food and water supplies is too widespread, and its toxic effects too well known, for continued inaction on this problem.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1623
EPA Comment ID: 20549
EPA Comment Code: 6120

Comment: It is a failure in your role to protect the people of the US that you want to no longer regulate perchlorate. The point at which you will begin to regulate it again in the future will most likely be because of a tragic foreseen incident. We all know that awareness, prevention, and action now prevents future complications. Please do the right thing and act accordingly.

Response: See response to comment code 6120.

Commenter Name: D. Brown
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1624
EPA Comment ID: 20550
EPA Comment Code: 6120

Comment: Please keep Perchlorate out of our drinking water. It is known to be harmful in very slight concentrations, and has been found in numerous water systems throughout the country. I urge the EPA to honor its responsibility to protect the public by regulating this substance.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1626
EPA Comment ID: 20551
EPA Comment Code: 6120

Comment: Please regulate perchlorate in our water. Your mandate is to protect the environment and the citizens of this country, and this kind of substance entering the bodies of children can't be permitted.

Response: See response to comment code 6120.

Commenter Name: Janet Ryan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1627
EPA Comment ID: 20552
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Please consider the harm that this decision could have on the public's health. Thank you. Janet Ryan

Response: See response to comment code 6120.

Commenter Name: M. A. Mulligan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1628
EPA Comment ID: 20553
EPA Comment Code: 6120

Comment: How can the EPA not regulate perchlorate in drinking water? It is known to impair the thyroid gland, affecting growth, development and metabolism, and it has been found in public water systems across the nation. I urge you to reverse this decision.

Response: See response to comment code 6120.

Commenter Name: J. Sprance
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1629
EPA Comment ID: 20554
EPA Comment Code: 6120

Comment: Why would you NOT regulate against Rocket Fuel in drinking water? I would like to understand what possible rationale there could be FOR allowing Rocket Fuel in drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1429
EPA Comment ID: 20557
EPA Comment Code: 6120

Comment: Really - there are enough health problems that need addressing in this country - autisim is just one example (I had never even heard of it as a child, currently though it's statistically on the increase). So, when there are health issues that can be addressed, and whose numbers can be keep lower, deregulation makes no sense. I'd like to hear anyone of you explain it to your children if your grandchild had mental retardation, or any other birth deficit, from the neglect you had in casting your vote against deregulation. Our clean waters must always be protected. Make your vote count - for the future generations! It may be your child and your grandchild that will be thanking you.

Response: See response to comment code 6120.

Commenter Name: Kathryn Murray
Commenter Organization: North Shore Unitarian Church
EPA Document ID: EPA-HQ-OW-2008-0692-1447
EPA Comment ID: 20558
EPA Comment Code: 6120

Comment: Keep our drinking water clean!

Response: This is not a comment, a response is not necessary.

Commenter Name: Nancy Yoke
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0621
EPA Comment ID: 20559
EPA Comment Code: 6120

Comment: Water Docket Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Ave., NW Washington, DC 20460

Docket Identification (ID) Number: EPA-HQ-OW-2008-0692 Preliminary Regulatory Determination on Perchlorate Re: Request for extension of comment period

I have a friend whose son was just diagnosed with Hashimoto's Disease, a disease of the thyroid. This is a potentially serious condition brought on by what? -- He is only 16! He has nodules on his thyroid -- something is causing this problem and since he lived on a naval base for several years, he has been exposed to this awful chemical Perchlorate in larger doeses. THIS IS SERIOUS AND WE NEED OUR GOVERNMENT AGENCIES TO WAKE UP! Quit protecting those at fault and do the right thing -- PROTECT OUR CHILDREN!!!!

Response: See response to comment code 6120.

Commenter Name: Samuel A. L. Perry
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1604
EPA Comment ID: 20562
EPA Comment Code: 6120

Comment: Dear EPA Staff,

As a drinking water professional, I generally abhor new regulations, but a national MCL on perchlorate is one thing that makes sense to me. After all, it occurs in drinking water at levels of public health concern far more often than than nearly any other chemical regulated under the SDWA, the two notable exceptions are arsenic and nitrate. If the same logic applied to perchlorate were applied to TCE, TCE would never have been regulated.

Response: See response to comment code 6120.

Commenter Name: James Hartman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1631
EPA Comment ID: 20575
EPA Comment Code: 6120

Comment: Industrial chemicals do not belong in our water supply. Obviously it is not possible to eliminate all traces of such from the public water supply, but electing to NOT regulate perchlorate is irresponsible and threatens public health. There is ample evidence that, unregulated, this chemical poses a significant risk to the public. Please reverse your preliminary decision on this matter.

Thank you,

James Hartman

Response: See response to comment code 6120.

Commenter Name: Marc H Lavietes
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1633
EPA Comment ID: 20576
EPA Comment Code: 6120

Comment: Perchlorate is poison and should not be in drinking water.

Marc H Lavietes MD

Response: See response to comment code 6120.

Commenter Name: Andrea Kintree
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1635
EPA Comment ID: 20577
EPA Comment Code: 6120

Comment: To Whom It May Concern,

Please monitor and regulate/strictly limit the amount of perchlorate in the water. Only the government has the authority to keep an eye on these things. I look at what happens in other countries where things aren't regulated, or the government people don't do their jobs, and the water situation is a mess. I don't want that to happen here.

Respectfully submitted, Andrea Kintree

Response: See response to comment code 6120.

Commenter Name: Gladys Poorte
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1636
EPA Comment ID: 20578
EPA Comment Code: 6120

Comment: I live in Austin, Texas and have learned that Texas is one of the states where perchlorate is found in the water. I have a 20 year old daughter that has recently developed thyroid problems.

There is no genetic history of thyroid problems in our family. Perchlorate, even in small amounts can impair the thyroid gland.

I've also learned that developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

EPA agrees that perchlorate has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher.

I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Please, protect our children!!!

Gladys Poorte

Response: See response to comment code 6120.

Commenter Name: Edward Klutz
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1638
EPA Comment ID: 20579
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Edward Klutz

Response: See response to comment code 6120.

Commenter Name: Janet Draper
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1640
EPA Comment ID: 20580
EPA Comment Code: 6120

Comment: Dear Sir:

I hope you will reverse the preliminary decision of the EPA not to regulate perchlorate in drinking water. Such a decision does not protect me and millions of other Americans from a toxic substance. We rely upon you you to protect us.

Thank you for your consideration of my plea.

Sincerely,

Janet Draper 1825 Dunedin Ave. Duluth, MN 55803

Response: See response to comment code 6120.

Commenter Name: Laura Reiley
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1641
EPA Comment ID: 20581
EPA Comment Code: 6120

Comment: Please fight for the right to have regulations restricting what is allowed to be dumped into our water ways.

Perchlorate contamination in the drinking water is unexceptable at any level.

You are my voice and I am saying NO to perchlorate.

Kind Regards, Laura Reiley

Response: See response to comment code 6120.

Commenter Name: Janine Ambrose
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1645
EPA Comment ID: 20582
EPA Comment Code: 6120

Comment: My question?

Why do I even need to write you about putting rocket fuel in our water. We have elected you because of your intelligence and support of the people. Please observe what is coming in front of you, and do what is best for the people!

Thanks for your time, Janine Ambrose

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1646
EPA Comment ID: 20583
EPA Comment Code: 6120

Comment: I urge the EPA to reconsider and reverse their decision about Perchlorate. It is harmful to our population's health and should not be allowed in our drinking water.

Response: See response to comment code 6120.

Commenter Name: Beth Adams

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1648
EPA Comment ID: 20584
EPA Comment Code: 6120

Comment: Percholoriate must be regulated out of our drinking water and soon!

We all know the hazardous effects of this dangerous chemical. Let's ban its use and keep our water safe for all generations!

Thank you!

Beth Adams

Greenfield, MA

Response: See response to comment code 6120.

Commenter Name: Susan R. Kepner
Commenter Organization: New Hampshire House of Representatives
EPA Document ID: EPA-HQ-OW-2008-0692-1653
EPA Comment ID: 20585
EPA Comment Code: 6120

Comment: As a state representative serving on the Resources, Recreation, and Development commitee in the NH House, I am very concerned about the quality of our drinking water. I cannot understand your decision NOT to regulate the dangerous "perchlorate" in drinking water. Please re-think this and remember that YOU are supposed to be guarding the health and welfare of all Americans!! Rocket fuel is not healthy in any thing we drink!! Even low levels are a danger, especially to infants and fetuses! Who will benefit by this lack of regulation? What big business or agency is MORE IMPORTANT THEN THE HEALTH OF THE AMERICAN PUBLIC???? REGULATE PERCHLORATE!!!!!!

Response: See response to comment code 6120.

Commenter Name: S. Broder
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1656
EPA Comment ID: 20586
EPA Comment Code: 6120

Comment: It's important to me that I can trust that our drinking water is clean and healthy, especially for my baby and small child, whose developing bodies are particularly vulnerable to chemicals.

Response: See response to comment code 6120.

Commenter Name: L. Thorp

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1660
EPA Comment ID: 20587
EPA Comment Code: 6120

Comment: why can't we find a way for jet planes to remove excess fuel from their tanks without dumping the fuel on the ground? Sounds so simple, then we would not have dangerous levels of perchlorate in the ground water. I am apalled that this practice goes on. Your inept ability to see that this is a very real concern for people also amazes me. Pardon my forwardness, but my husband died from something related to this, and I am concerned that others may die needlessly because regulations are not either followed, or not created for the military which is the largest polluter in this country, and largest contributor to superfund sites throughout the country. My husband was an environmental engineer who worked on a superfund site, and I know first hand about groundwater contamination. His job was to clean up the sites! Please reconsider the measure that is being forwarded very seriously.

Response: See response to comment code 6120.

Commenter Name: Jimmy Spearow
Commenter Organization: Sacramento Chapter, Physicians for Social Responsibility
EPA Document ID: EPA-HQ-OW-2008-0692-1672
EPA Comment ID: 20591
EPA Comment Code: 6120

Comment: We urge you to protect Americans' health by regulating perchlorate in drinking water in accordance with the Safe Drinking Water Act. Please set the MCL for perchlorate in drinking water at no greater than 1 ppb.

Several states, including New Jersey, Massachusetts, and California have already addressed the issue of perchlorate in drinking water by either already setting or planning to set a MCL that is far lower than the current EPA recommendation. While none of these states have proposed a MCL as low as 1 ppb, their standards would still be far more protective of public health than the current EPA recommendation. But beyond these state borders, millions of people drink perchlorate contaminated water and depend on the federal government to protect them. EPA must fulfill this responsibility. Please regulate perchlorate in drinking water at no greater than 1 ppb.

Sincerely,

Jimmy Spearow, Ph.D. Sacramento Chapter, Physicians for Social Responsibility 911 Pennsylvania Place, #3 Davis, CA 95616 jlspearow@sbcglobal.net

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1673
EPA Comment ID: 20592
EPA Comment Code: 6120

Comment: This decision should be reversed. The public has the right to know what is in their drinking water. Think about our children and grandchildren. I want them to be healthy and to be aware of what they are putting in their bodies. Keep our water safe.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1674
EPA Comment ID: 20593
EPA Comment Code: 6120

Comment: Hi, I am an ordinary citizen, but an educated one, and I am very dismayed at the idea that the EPA may not regulate perchlorate. I urge the EPA to continue to regulate this substance, which can be very detrimental to a human's thyroid gland and even more serious to children that are exposed. Keep our water clean! It's bad enough we have to deal with several exposures and pollutions.

Thank you.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1676
EPA Comment ID: 20594
EPA Comment Code: 6120

Comment: For heaven's sake, STOP THE MADNESS.....D you honestly think that this is okay.....Clean it up please and then keep it clean....No perchlorate in out water and keep out the other cooties. Thank you

Response: See response to comment code 6120.

Commenter Name: J. Mosman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1682
EPA Comment ID: 20595
EPA Comment Code: 6120

Comment: Please re-consider your preliminary decision regarding perchlorate in drinking water. We need to protect our water resources; they are much more important than oil, gas, and coal! Without water of good quality, we will be faced with impossible problems, and it might be too late to correct them. Let's be pro- active, limit the amounts of perchlorate to an extremely tiny percentage, and not realize years from now there was a horrendous mistake made.

We definitely need to protect future generations from problems associated with perchlorate, which links have been proven to exist.

Please, do revise your position; water is essential, and it's been badly abused in the past. We definitely need to re-orient ourselves and protect our resources - our nation's well-being relies on it.

Response: See response to comment code 6120.

Commenter Name: N. Abercrombie
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1685
EPA Comment ID: 20596
EPA Comment Code: 6120

Comment: Please enact legislation that will protect our freshwater system from contamination with pollutants.

Response: This is not a comment, a response is not necessary.

Commenter Name: J. Miller
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1689
EPA Comment ID: 20597
EPA Comment Code: 6120

Comment: Please reverse your decision to not regulate perchlorate in drinking water. Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought. I am concerned for my family and the environment.

Response: See response to comment code 6120.

Commenter Name: P. Paul
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1691
EPA Comment ID: 20598
EPA Comment Code: 6120

Comment: This request is to ask you to seriously consider reversing your decision not to consider regulating perchlorate in drinking water. Since perchlorate is used for rocket fuel and studies have shown trace amounts can destroy the thyroid gland as well as thyroid inhibition in fetuses, the long-range costs for health care is phenomenal. From a logical perspective, it makes more sense to regulate perchlorate in drinking water before it becomes a national health and environmental diaster. Thank You

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-1692
EPA Comment ID: 20599
EPA Comment Code: 6120

Comment: As a tax payer, I urge the government/EPA to continue the regulation of perchlorate in our drinking water. Our planet/bodies is already subjected to enough unregulated contaminates..... keep our drinking water as pure/safe as possible!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1695
EPA Comment ID: 20600
EPA Comment Code: 6120

Comment: regulate perchlorate period.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1697
EPA Comment ID: 20601
EPA Comment Code: 6120

Comment: Rocket fuel (perchlorates) wasn't an original ingredient of water and shouldn't be in it now! You can add it to your own water if you wish. However, I'd greatly appreciate your leaving it out of mine. Your job is to help protect the public, NOT big business.

Response: See response to comment code 6120.

Commenter Name: Lesley LeFevre
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1698
EPA Comment ID: 20602
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. -Lesley LeFevre, PsyD

Response: See response to comment code 6120.

Commenter Name: Clark Sellars
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1699
EPA Comment ID: 20603
EPA Comment Code: 6120

Comment: I urge the EPA to Regulate Perchlorate in our drinking water. If you don't do it NOW, it will have to be in the future costing ten times as much and many more water supplies degraded. Please think of the health of the public and the enviroment FIRST. Sincerly Clark Sellars

Response: See response to comment code 6120.

Commenter Name: L. Helfman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1700
EPA Comment ID: 20604
EPA Comment Code: 6120

Comment: You should regulate perchlorate in our water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1701
EPA Comment ID: 20605
EPA Comment Code: 6120

Comment: Gentlemen,

Higher perchlorate levels in drinking water? You have got to be kidding. Rocket fuel does not belong in drinking water, at any level!

Perchlorate is proven harmful to developing fetuses, infants and children and at lower levels than previously thought. Allowing perchlorate in drinking water is filfully negligent on your part.

Please fulfill your responsibility to the people and environment. Performing your duty under the law if a very important job; please do not shirk it now.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1702
EPA Comment ID: 20606
EPA Comment Code: 6120

Comment: I am very concerned about allowing any perchlorate into the water system. Please regulate this chemical and protect our water system. Thank you.

Response: See response to comment code 6120.

Commenter Name: Anonymous

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1703
EPA Comment ID: 20607
EPA Comment Code: 6120

Comment: I SUPPORT THIS COMMENT IN FULL. EPA HAS BEEN APPROVING FAR TOO MANY TOXIC POLLUTANTS FOR THE LAST 17YEARS, TURNING DOWN NONE FOR APPROVAL. THAT SHOWS NO DISCRIMINATINO ON THE PART OF THIS AGENCY AND NO PROTECTION FOR THE AMERICAN PUBLIC AND ITS CHILDREN.

Response: This is not a comment, a response it not necessary.

Commenter Name: Paul Einboden
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1704
EPA Comment ID: 20608
EPA Comment Code: 6120

Comment: Please reconsider the preliminary determination on setting a regulation for perchlorate in drinking water.

It is critical that harmful chemicals are not in the public drinking water. (That perchlorate not work its way into further drinking water systems).

Thank you Paul Einboden St. Petersburg, FL

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1707
EPA Comment ID: 20609
EPA Comment Code: 6120

Comment: I respectfully request that the EPA regulate perchlorate levels in water. There are certain chemicals that are permissible in the water supply; this is not one of them.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1708
EPA Comment ID: 20610
EPA Comment Code: 6120

Comment: Please make the regulations stricter for the purity of our drinking water. There has been a substantial increase in childhood autism and other ailments in the last 20 years. Studies are continuing to try and find the causes of this, but why wait for the results to show that higher levels

of toxins in the drinking water are to blame. Please, please be proactive in keeping the health and welfare of our children.

Response: See response to comment code 6120. Commenter's statements are out of scope of this regulatory action.

Commenter Name: MattHew C. Ford, Jr.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1710
EPA Comment ID: 20611
EPA Comment Code: 6120

Comment: To Whom It May Concern,

Keep Perchlorate out of our drinking water.

Very truly yours,

MattHew C. Ford, Jr., M.P.A.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1713
EPA Comment ID: 20612
EPA Comment Code: 6120

Comment: No rocket fuel/Perchlorate in drinking water, please.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1716
EPA Comment ID: 20613
EPA Comment Code: 6120

Comment: We do NOT want perchlorate in our drinking water!!!!!!! PLEASE don't be responsible for it happening.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1719
EPA Comment ID: 20614
EPA Comment Code: 6120

Comment: Perchlorate is a chemical we know is harmful. Why would it be a lawful option to allow a chemical used in rocket fuel in drinking water? The chemical can impact human development and metabolism, even at low levels. Please consider our children and America's coming generations. Regulate Perchlorate in our drinking water and turn the decision to allow it around.

Response: See response to comment code 6120.

Commenter Name: S. Ultimo
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1722
EPA Comment ID: 20615
EPA Comment Code: 6120

Comment: why is there any question on whether perchlorate should be regulated in drinking water ?

Response: This is not a comment, a response is not necessary.

Commenter Name: Carol Bigelow
Commenter Organization: University of Massachusetts
EPA Document ID: EPA-HQ-OW-2008-0692-1427
EPA Comment ID: 20633
EPA Comment Code: 6120

Comment: Accordingly, docket ID No. EPA-HQ-OW-2008-0692 should not form the basis for national primary drinking water regulation.

Considering these issues, we conclude that EPA has based its argument for not regulating perchlorate contamination in public water systems on a literature that is both limited and ill focused. We believe that EPA has not performed a sufficiently "thorough review" of the literature, that it has omitted important information, and that it has failed to perform its due diligence in the interpretation and analysis of the information that it did present. To correct this, EPA must employ the CDC study (Blount et al, 2006a) as the point of departure for RfD determination, and must focus on the neonate and infant as the most sensitive population.

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Response: EPA has determined to regulate perchlorate in drinking water (See response to comment code 6120). For further information about the RfD for perchlorate, please see the response to comment ID 28927 under comment code 2110. Regarding the comment for EPA to focus on the neonate and infant as the most "sensitive population," EPA published a Federal Register notice on August 19, 2009 seeking comments on additional approaches to analyzing data related to EPA's perchlorate regulatory determination. These comments were sought in an effort to ensure consideration of all the potential options for evaluating whether there is a meaningful opportunity for human health risk reduction of perchlorate through a national primary drinking water rule which included neonates and children.

Commenter Name: Robert Howd
Commenter Organization: California Environmental Protection Agency, Water Toxicology Section
EPA Document ID: EPA-HQ-OW-2008-0692-1671
EPA Comment ID: 20652
EPA Comment Code: 6120

Comment: We hereby petition EPA to rethink their alleged health-protective level for perchlorate, and their proposed decision not to regulate it in drinking water. Thank you for consideration of our comments.

Sincerely yours,

Robert A. Howd, Ph.D. Senior Toxicologist

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Response: See response to comment code 6120.

Commenter Name: Mic Stewart
Commenter Organization: Metropolitan Water District of Southern California
EPA Document ID: EPA-HQ-OW-2008-0692-1784
EPA Comment ID: 20662
EPA Comment Code: 6120

Comment: In 2004, California's Office of Environmental Health Hazard and Assessment (OEHHA) adopted a public health goal (PHG) for perchlorate of 6 ppb. In October 2007, the California Department of Public Health (CDPH, formerly the Department of Health Services) adopted a primary drinking water standard (maximum contaminant level, MCL) of 6 ppb.

Although California has its own MCL for perchlorate, a national drinking water standard would assist in the clean-up of hundreds of U.S. Department of Defense facilities in Southern California and around the country. Since the detection of perchlorate contamination throughout the southwest Region and in hundreds of local groundwater wells, Metropolitan, its member agencies, and the drinking water community have called on the EPA to make a regulatory determination on perchlorate consistent with the tenets of the Safe Drinking Water Act.

Metropolitan wishes to offer the following comments:

* Regulatory Determination - With EPA's determination not to regulate perchlorate and therefore not set a drinking water MCL, Metropolitan is concerned that without Federal regulation potential clean-up efforts of contaminated surface and groundwater sites throughout the region and other parts of the Country may be impaired.

Response: See response to comment code 6120.

Commenter Name: Stephen A. Owens
Commenter Organization: Arizona Department of Environmental Quality
EPA Document ID: EPA-HQ-OW-2008-0692-1785
EPA Comment ID: 20666
EPA Comment Code: 6120

Comment: Numerous environmental, health and medical agencies, including the National Academy of Sciences, have documented and agreed that ingesting perchlorate through contaminated water, food and human breast milk may interfere with the production of thyroid hormones. This interference occurs because perchlorate "competes" with the uptake of iodide in the thyroid gland. Adding to this concern is EPA's own finding that the risk to infants is greater even when they have ingested low levels of perchlorate. Finally, the Centers for Disease Control found that ingesting perchlorate contaminated food and water may pose even a greater health threat for those women who have lower iodine intake levels to begin with.

Based upon the known occurrences of perchlorate in Arizona's water supply coupled with known human health concerns at detected levels, ADEQ disagrees with EPA's preliminary decision not to regulate perchlorate and strongly encourages EPA to reconsider the determination.

Thank you in advance for your consideration of these comments

Sincerely, Stephen A. Owens Director

Response: See response to comment code 6120.

Commenter Name: Ann Ell
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1522
EPA Comment ID: 20668
EPA Comment Code: 6120

Comment: To Whom it May Concern, As a Mother of two small children who had to deal with this problem recently, I urge you to take a good look at the regulations and make them as forceful as possible. sincerely, Ann M. Ell Tewksbury MA

Response: See response to comment code 6120.

Commenter Name: P. Impink
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1434
EPA Comment ID: 20675

EPA Comment Code: 6120

Comment: Our whole town was not able to drink the water for 6 months when perchlorate was detected from discharge from another community. I was pregnant at the time. Please require municipal water suppliers to test for perchlorate. We just don't know the long term health effects of these contaminants.

Response: See response to comment code 6120.

Commenter Name: Sandra Clifford Teeple
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1730
EPA Comment ID: 20677
EPA Comment Code: 6120

Comment: I am deeply concerned by the EPA's decision to allow perchlorate in public drinking water. While allowing this substance to remain may be an initial cost- saving issue for some businesses, in the long term, perchlorate COSTS America a great deal of money, time, effort, and resources. The damage to infants and small children is incalculable; the costs to medically care for and to remedially educate the children damaged by deliberate pollution, such as perchlorate, are also incalculable.

Prevention is always CHEAPER than restoration and remediation! Please do not permit the pollution of our drinking water. Thank you for listening to my concerns.

Sandra Clifford Teeple jsteep@aol.com

Response: Please See response to comment code 6120.

Commenter Name: Karen A. Vilandry
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1734
EPA Comment ID: 20680
EPA Comment Code: 6120

Comment: Dear Mr. Johnson,

With respect to the decision in Massachusetts to lower the perchlorate standard in drinking water, it only makes sense to do the same nationwide.
http://www.boston.com/news/local/massachusetts/articles/2006/07/28/massachusetts_sets_state_standard_for_perchlorate/?p1=email_to_a_friend

Drinking water needs to be in its purest form to protect public health. Please keep in mind, that already two thirds of the country is using hydrofluosilicic acid, (fluoride), a hazardous waste byproduct of the phosphate industry, in drinking water. By allowing another toxic chemical in the drinking water, it only exacerbates the problem even further creating quite a toxic cocktail of chemicals that humans don't need in their water source. Please act on behalf of all, protect the population and keep the water clean.

Thank you! Karen A. Vilandry "Wasted Away"

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1738
EPA Comment ID: 20682
EPA Comment Code: 6120

Comment: Please reverse your decision on allowing the rocket fuel addative to be allowed in our drinking water.

Thank you.

Response: See response to comment code 6120.

Commenter Name: Denis Orpen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1739
EPA Comment ID: 20683
EPA Comment Code: 6120

Comment: I have learned the dangers of perchlorate and ask you to help keep the requirement intact for our drinking water.Removal of the testing would eliminate detection in case of contamination. We in Tewksbury still recall the contamination of our water in 2004.

Denis Orpen 51 Nina Dr Tewksbury

Response: This regulatory action does not address any existing testing requirements for perchlorate in local jurisdictions. Please see response to comment code 6120.

Commenter Name: L. Kuegler
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1740
EPA Comment ID: 20684
EPA Comment Code: 6120

Comment: The testing of water for perchlorate is very important. As a resident of Tewksbury,MA I was subject to contaminated perchlorate drinking water and during that time I contracted hyperthyroidism. This has affected my life drastically.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1744

EPA Comment ID: 20686
EPA Comment Code: 6120

Comment: testing for perchlorate is very important and should not be discontinued. I live in Tewksbury, Ma. We were unable to drink our water for months because of high levels of perchlorate. I have young children so my concern is for them.

The side effects of perchlorate are scary so please do what is right and continue to test!

Response: This regulatory action does not address testing requirements for perchlorate in local jurisdictions. Please see response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1745
EPA Comment ID: 20687
EPA Comment Code: 6120

Comment: Although perchlorate levels have perhaps dropped to neglible levels in water supplies as a whole, in 2004 the tap water in Tewksbury, Massachusetts could not be consumed because of elevated perchlorate levels. In fact, this condition was ultimately isolated to dumping by a manufacturing facility upstream on the Concord River, which merges with the Merrimack River, from which Tewksbury's water is drawn. It has since been addressed, but consider the implications for residents of Tewksbury, and specifically for children, had the condition not been detected, I don't believe this is a reasonable risk to assume. I certainly would not want my three small children to be harmed by such a decision.

Thank you.

Resident of Tewksbury

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1746
EPA Comment ID: 20688
EPA Comment Code: 6120

Comment: Please continue to test for Perchlorate and other chemicals in our drinking water. Right around the time the perchlorate was found, my neighbor was very sick with thyroid problems (in her 40s) and I had to have chemotherapy at age 41 from a molar preganancy turned choriocarcinoma.

People's health is nothing to mess around with. Health is wealth and we can't afford not to have clean air in water. Please be sure to test our water!

MANY THANKS.

A concerned citizen of Tewksbury

Response: This regulatory action does not address testing requirements for perchlorate in local jurisdictions. Please see response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1747
EPA Comment ID: 20689
EPA Comment Code: 6120

Comment: umm how about we tighten water safety standards rather than making them more lax. Don't be [expletive] retarded.

Response: This is not a comment, a response is not necessary.

Commenter Name: S. Franzeen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1753
EPA Comment ID: 20690
EPA Comment Code: 6120

Comment: Perchlorate is a nasty little chemical. I'm not sure what the EPA's motivation is to not regulate the threat of perchlorate in our drinking water, but please add my voice in opposition to such a notion. Perchlorate must be regulated.

Response: See response to comment code 6120.

Commenter Name: E. Cruz
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1755
EPA Comment ID: 20691
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. I live near a plant which releases perchlorate into the environment every day, and it is an ongoing concern for me and my family.

Response: See response to comment code 6120.

Commenter Name: Bruce P. Boxer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1756
EPA Comment ID: 20692
EPA Comment Code: 6120

Comment: Please keep our water safe to drink. Regulate Percholates. Please Thanks, Bruce

Response: See response to comment code 6120.

Commenter Name: Ylana Stewart
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1757
EPA Comment ID: 20693
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Perchlorate is used in rocket fuel, flares, and explosives. How can we possibly allow it to exist in our drinking water? The same water that our children drink. It is horrifying to think that the EPA does not consider regulation extremely important. Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. Please protect us from this hazard. Sincerely, Ylana Stewart - Rockland, Massachusetts

Response: See response to comment code 6120.

Commenter Name: D.L. Humes
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1759
EPA Comment ID: 20694
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on not regulating for perchlorate in drinking water.

There is enough evidence showing a strong correlation between perchlorate and health problems. Please do the job your department was created for and protect the citizens of this country and the environment instead of large corporations and bowing to special interests that influence your department either directly or through congressmen who have been bribed through campaign funds. Pass regulations that will protect us today and tomorrow.

Response: See response to comment code 6120.

Commenter Name: Lynn Brown
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1760
EPA Comment ID: 20695
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary decision on perchlorate levels in drinking water. This stuff has health impacts even at low levels.

Young children would be especially be at risk. Please protect the public health. Let's move forward... not backward.

Lynn Brown 18 Foxcroft Rd. Niantic, CT

Response: See response to comment code 6120.

Commenter Name: Heather Hesse-Stromberg
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1763
EPA Comment ID: 20696
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Heather Hesse-Stromberg
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1763
EPA Comment ID: 20698
EPA Comment Code: 6120

Comment: As the mother of a 4 year-old, this kind of potential hazard frightens me to the core. There are enough threats to her good health and normal development without adding the one thing she is most encouraged to do (drink lots of water) to the list...

Please reconsider your decision to not regulate perchlorate in the drinking water - the health of the next generation depends on it!

Heather Hesse-Stromberg Rochester, NH

Response: See response to comment code 6120.

Commenter Name: D. Peters
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1764
EPA Comment ID: 20699
EPA Comment Code: 6120

Comment: I am writing to urge the EPA to protect public health by increasing regulation of perchlorate in drinking water. Contamination can put may children and adults at risk for serous health problems.

Response: See response to comment code 6120.

Commenter Name: Agnes Merrick
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1771

EPA Comment ID: 20700
EPA Comment Code: 6120

Comment: To the EPA,

I am deeply concerned over your unethical attitude towards allowing perchlorate to contaminate our drinking water. If one of your own family members suffered a life-threatening disease or an incurable deformity from ingesting Rocket Fuel- tainted water, you would have to live with the fact that your moral laziness was the precipitating cause.

Sincerely, Agnes Merrick 519 Yarmouth Rd. Baltimore, Md. 21286

Response: This is not a comment, a response is not necessary.

Commenter Name: N. Thakur
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1772
EPA Comment ID: 20701
EPA Comment Code: 6120

Comment: ban perchlorate in drinking water

Response: See response to comment code 6120.

Commenter Name: S. Blackard
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1774
EPA Comment ID: 20702
EPA Comment Code: 6120

Comment: As a citizen of the United states I count on the EPA to set regulations that keep our drinking water clean and healthy. Please set regulations to keep perchlorate and other potentially toxic chemicals out of our drinking water!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1777
EPA Comment ID: 20703
EPA Comment Code: 6120

Comment: Clean drinking water is a limited natural resource - fought over in some regions - and is worthy of the full protection by the EPA. We must ensure that all business enterprises and municipalities are held to the highest siting and operating standards necessary to safeguard our water supplies. Of particular concern to me is the possibility of water contamination by perchlorate - an ingredient in rocket fuel. This must not be allowed to take place and the EPA must set strict contamination and testing guidelines.

Response: See response to comment code 6120.

Commenter Name: Becky
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1778
EPA Comment ID: 20704
EPA Comment Code: 6120

Comment: I am concerned about keeping our water safe and about allowing perchlorate intoour water supply. I believe that we should not have any perchlorate in our water. Becky

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #7 – Group Unidentified
EPA Document ID: EPA-HQ-OW-2008-0692-1518
EPA Comment ID: 20705
EPA Comment Code: 6120

Comment: I understand the dangers of perchlorate and ask you to keep the testing requirement intact for our public drinking water supplies. Removal of the testing requirement would eliminate detection of perchlorate in the case of accidental or intentional contamination of drinking water supplies, such as the Tewksbury Massachusetts contamination in 2004.

Response: See response to comment code 6120.

Commenter Name: Daniel Green
Commenter Organization: Green Machine Consulting, LLC
EPA Document ID: EPA-HQ-OW-2008-0692-1783
EPA Comment ID: 20706
EPA Comment Code: 6120

Comment: This is a dumb rule. Please reject it.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1790
EPA Comment ID: 20707
EPA Comment Code: 6120

Comment: Test for and keep perchlorate out of our drinking water.

Response: See response to comment code 6120.

Commenter Name: L. McPhedran
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-1791
EPA Comment ID: 20708
EPA Comment Code: 6120

Comment: Please do not allow perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Karen Parelhoff
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1793
EPA Comment ID: 20709
EPA Comment Code: 6120

Comment: I do not understand why you would not insist on regulating perchlorate in our water. I do not want rocket fuel in my drinking water in any amount, truthfully. At the very least I want it monitored and regulated. We know that there are health concerns associated with it especially for the unborn. Please put country first that means the health and well-being of our children and the rest of us should be your first concern. It irks me that I need to write this as it seems like such a no-brainer. Protect our water. Protect our health.

Karen Parelhoff 6803 Glenmont St. Falls Church, Va. 22042

Response: See response to comment code 6120.

Commenter Name: L. Astur
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1803
EPA Comment ID: 20711
EPA Comment Code: 6120

Comment: I urge the EPA to protect public health by regulating perchlorate in drinking water.

This substance has been found in public drinking water supplies nationwide and is a serious threat the the health of fetuses, children, and adults.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1808
EPA Comment ID: 20712
EPA Comment Code: 6120

Comment: I hope you do not deregulate the amount of perchlorate in drinking water. The drinking water should be clean to drink, not have trace amounts of rocket fuel in it.

Response: See response to comment code 6120.

Commenter Name: Ed O. Travis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1810
EPA Comment ID: 20713
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Perchlorate is a dangerous chemical, and the EPA owes citizens a decision base on the best available scientific data, with a margin of safety added to ensure protection of the public health in situations where there is not a consensus.

Ed Travis Austin, TX

Response: See response to comment code 6120.

Commenter Name: Sierra Club
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1811
EPA Comment ID: 20714
EPA Comment Code: 6120

Comment: Please re-visit. No perchlorate in water!

Response: See response to comment code 6120.

Commenter Name: Elanne Palcich
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1812
EPA Comment ID: 20715
EPA Comment Code: 6120

Comment: As a citizen living within the U.S.A., I prefer not to have perchlorate in my water. I hope the EPA doesn't think it's ok to have perchlorate leaching into our water supplies. There must be some sort of EPA policy guidelines in place to protect citizens from toxic chemicals such as this. The issue seems to be following through with your mandate.

Thanks. Elanne Palcich 29 SE 5th St. Chisholm, MN 55719

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1813
EPA Comment ID: 20716
EPA Comment Code: 6120

Comment: Allowing such things as percolate, fluoride, drugs and other toxins in the water is rediculous. Do your job and protect the populous from these and other toxins.

Response: Regarding regulating perchlorate in drinking water, see response to comment code 6120. Regarding regulation of "fluoride, drugs and other toxins in the water," no response is necessary as it is outside of the scope of this action.

Commenter Name: Laurie Meisenheimer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1814
EPA Comment ID: 20717
EPA Comment Code: 6120

Comment: Please, do as you need to and protect the environment for the people of the United States. That is your job. You need to reverse your decision not to regulate percholate. It would be negligent not to try to keep our waters free of this known dangerous chemical. As a teacher, I see many children who are not funtioning as they should. We need to do our best to keep them whole and healthy. Regulate percholate- keep us safe. That is what the EPA is for, and we all look to you to do what is right.

Laurie Meisenheimer First Grade Teacher

Response: See response to comment code 6120.

Commenter Name: T. Morris
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1815
EPA Comment ID: 20718
EPA Comment Code: 6120

Comment: On October 10, the EPA announced its preliminary decision not to regulate perchlorate in drinking water. Please reverse this decision and keep our water clean!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1817
EPA Comment ID: 20719
EPA Comment Code: 6120

Comment: Even if at any point in time percolate isn't much of a threat it is possible that someone somewhere could have access to it and if it ends up in the water, not only would everyone want it detected but also somebody could be caught for illegal activity.

Response: No response necessary, this is not a comment.

Commenter Name: Regina Epp

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1820
EPA Comment ID: 20720
EPA Comment Code: 6120

Comment: To whom it may concern:

Regarding the allowance of perchlorate in drinking water--Please note that this substance affects metabolism at much lower levels that previously thought. I strongly urge you to protect our drinking water supply, which is quickly deteriorating in quality, from further contamination. My family and I are putting our faith in our government's assertion that the needs of ordinary people will not suffer when balanced with the desires of corporations.

Sincerely,

Regina Epp

Response: See response to comment code 6120.

Commenter Name: Noel Anderson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1822
EPA Comment ID: 20721
EPA Comment Code: 6120

Comment: This is in regards to allowing percholate in our drinking water and not regulating it. As a person who has thyroid problems, I am highly concerned that the government would allow a chemical into our drinking water that would further compromise my health. For this reason I strongly urge you to ban percholate entirely from our water.

Sincerely,

Noel Anderson Quakertown, PA

Response: See response to comment code 6120.

Commenter Name: S. Elliott
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1823
EPA Comment ID: 20722
EPA Comment Code: 6120

Comment: NO PERCHOLATE in our drinking water!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-1824
EPA Comment ID: 20723
EPA Comment Code: 6120

Comment: Please reverse your preliminary determination concerning the amount of perchlorate in our drinking water. Our children have enough to face due to our poor choices. The wellness of our generation and those that follow will be directly affected by this decision and those similar. It is time we stop adding any chemicals that are not absolutely necessary to that which we ingest. There are other ways to solve these problems without exasperating our contribution to illness.

Response: See response to comment code 6120.

Commenter Name: Lois Fournier
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1825
EPA Comment ID: 20724
EPA Comment Code: 6120

Comment: As a nurse for 40 years, I am concerned about public health. Clean water and clean air are basic rights that MUST be protected for the health of all peoples. To allow toxic chemicals like perchlorate in our drinking water at levels that cause problems, especially to those who are most vulnerable, is criminal. We can't expect to have productive citizens whose health is compromised. And we will burden society even more with costly, lifelong medical bills. Please toughen the laws on acceptable levels of perchlorate for everyone's sake.

Lois Fournier Centerville, MA

Response: See response to comment code 6120.

Commenter Name: Robert A. Cloutier, Jr.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1832
EPA Comment ID: 20725
EPA Comment Code: 6120

Comment: Please regulate perchlorate in drinking water. I do not want rocket fuel in my drinking water.

Thank you, Robert A. Cloutier, Jr.

Response: See response to comment code 6120.

Commenter Name: M. Killian
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1834
EPA Comment ID: 20726
EPA Comment Code: 6120

Comment: Please regulate our drinking water. Tell the EPA to keep perchloate out of the water. Do not allow jet fuel to seep into our supplies!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1837
EPA Comment ID: 20727
EPA Comment Code: 6120

Comment: Please regulate and monitor drinking water for perchlorate contamination.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1839
EPA Comment ID: 20728
EPA Comment Code: 6120

Comment: We should be tightening the standards for drinking water, not loosening them. Americans deserve safe, potable drinking water.

Response: See response to comment code 6120.

Commenter Name: Michael Peterson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1841
EPA Comment ID: 20730
EPA Comment Code: 6120

Comment: October 28, 2008 Water Docket Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Ave., NW. Washington, DC 20460.

Dear Sir or Madam,

I live in Los Angeles, CA and like many who live here, I am greatly concerned with the level of perchlorate in our water supply due to rocket fuel spillage. These worries have doubled recently as my wife and I are now planning to have our first child.

While I understand there is conflicting evidence when it comes to the study of perchlorate, it is widely accepted that percholorate can negatively affect the thyroid in a mother which is essential for proper development of the fetal brain.

No woman in the United States should be scared to drink tap water because she thinks it might cause damage to her unborn child. Rocket fuel has no place in our drinking supply IN ANY LEVEL - and certainly not at an increased level from what we used to believe was acceptable.

I trust you to do the right thing and require those who spill harmful chemicals in our water to pay for proper cleanup - and to keep "acceptable" levels of perchlorate as low as humanly possible.

Sincerely yours, Michael Peterson

Response: Regarding regulating perchlorate in drinking water, see response to comment code 6120. Regarding "requiring those who spill harmful chemicals in our water to pay for proper cleanup," see response to comment code 6300.

Commenter Name: C. Rose
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1842
EPA Comment ID: 20731
EPA Comment Code: 6120

Comment: Please do whats right

Response: No response necessary, this is not a comment.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1843
EPA Comment ID: 20732
EPA Comment Code: 6120

Comment: It is always astonishing how the people that pledged to defend the American people, plan to allow toxins and carcinogens flow through our drinking water. For what? A favor? My first child is due at the end of April. When you go to sleep tonight, think about my child and the regulations you are attempting to abandon. I wouldn't allow anyone to ever poison your child, why would you allow the poisoning mine? Why do you want to poison children? How can you live with yourself? My child, crying, because he has been poisoned thanks to your support of deregulation policies.

Response: No response necessary, this is not a comment.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1844
EPA Comment ID: 20733
EPA Comment Code: 6120

Comment: I grew up on Redstone Arsenal in Alabama(Aka Rocket City) and know first hand how damaging this chemical can be. My mother has had thyroid problems ever since my family moved there in 1984. Even though we only lived there for 5 years, and have zero history of thyroid problems in the family, she is now on medication for thyroid problems, and will be for the rest of her life.

To think that 20 years later, there is still zero regulation on Perchlorate is not only idiotic, but it is harming human health... The EPA has become a joke if you ask me under the Bush administration's last 8 years. It is their legal responsibility to protect American's from environmental harm, and yet here they are doing the exact opposite..

Why do i even pay taxes if this is what we get for our money? Should we honestly keep paying you to harm our loved one's health?

This government needs to move back to being FOR the people, and NOT for the Corporations....

Response: No response necessary, this is not a comment.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1845
EPA Comment ID: 20734
EPA Comment Code: 6120

Comment: I'm going to keep this as short and simple as possible.

Americans as a whole are terribly overweight and have a tendency to put more than enough things into our bodies with a negative effect associated with them,

Why would we not want to clean up our water as much as we can, especially if we can remove a cause of tyroid problems in children, unborn children and their mothers.

It only makes sense to be willing to spend the time and money to better our water for the lives of our children.

Response: No response necessary, this is not a comment.

Commenter Name: Kenneth C. Moore
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1846
EPA Comment ID: 20735
EPA Comment Code: 6120

Comment: Put the allowable limits of Perchlorate in drinking water back to what it was in 2002. I don't care what it costs to clean up; human beings, especially newborns, should not have to be exposed to the potential health reprocussions of this matter. It shall be the U.S. Government's #1 priority to PROTECT and SERVE the citizens of the United States. Until the U.S. Government stops being persuaded by special interest groups, this country is NEVER going to see what it is truly capable of becoming; it will never see its TRUE potential.

Kenneth C. Moore

Response: See response to comment code 6120.

Commenter Name: Dennis W.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1849
EPA Comment ID: 20738
EPA Comment Code: 6120

Comment: I think there should be stronger regulations on Perchlorate and a law that requires a clean up should be enacted.

I lived next to a military base for 5 years and my wife went through three different pregnancies at that time. My research shows that Perchlorate can cause thyroid problems in pregnant women. During my wife's last pregnancy she developed a thyroid problem. My wife has to deal with a thyroid problem and we have to pay for thyroid medication for the rest of our lives possible because the EPA doesn't know how to do their job. There needs to be stronger legislation on this chemical. At least regulate it to the point of what was considered safe in 2002.

Thank You Dennis W.

Response: See response to comment code 6120.

Commenter Name: M. Biro
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1850
EPA Comment ID: 20739
EPA Comment Code: 6120

Comment: It is very important the the Agency is fully aware of the risks of allowing substances to be disposed in our water. It is expected that, while there is ANY doubt that harmful consequences may occur, the Agency void any additional permission. The Agency is supposed to always protect the interests of the population and never take any action for which the consequences are not fully understood, when authorizing the increase/release of chemicals on the environment. Therefore, based on your study, I do not believe the Agency has all the necessary elements to put this rule in effect, and it is the agency responsibility to void it.

Response: See response to comment code 6120.

Commenter Name: Charles Cronin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1852
EPA Comment ID: 20741
EPA Comment Code: 6120

Comment: In regards to the changes on rules regarding perchlorate levels in drinking water, I believe the new changes should apply to only the area in and around Crawford, Texas, leaving the higher and safer standards for the bulk of the US citizenry!

Thanks, Charles Cronin

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1853
EPA Comment ID: 20742
EPA Comment Code: 6120

Comment: Please stop your midnight regulations that harm the environment and people. Citizens are more important than lobbyists (they just have more money.) Please represent the little guys and do what is best for us.

Response: No response necessary, this is not a comment.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1854
EPA Comment ID: 20743
EPA Comment Code: 6120

Comment: Perchlorate should be regulated at a level at or lower than the standard set in 2002, or at the set standard in California, which ever is lower. Raising this level is counter productive.

Response: See response to comment code 6120.

Commenter Name: Mi Sunyn
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1861
EPA Comment ID: 20745
EPA Comment Code: 6120

Comment: 11/06/08

Dear EPA,

Please clean-up our water supply by restricting perchlorates

Mi Sunyn 110 Roberts Ave #201 Alexandria, VA 22076

Response: See response to comment code 6120.

Commenter Name: J. Agee
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1862
EPA Comment ID: 20746
EPA Comment Code: 6120

Comment: 11/06/08

Dear EPA,

Please do not put harmful chemicals in our water.

J. Agee 850 N. Randolph St. Arlington, VA 22202

Response: EPA does not intend to put harmful chemicals into our water, instead EPA has determined that perchlorate should be regulated in public water systems. See response to comment code 6120.

Commenter Name: Tony Frangello
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1863
EPA Comment ID: 20747
EPA Comment Code: 6120

Comment: 5 NOV 08

TO WHOM IT MAY CONCERN

I WOULD LIKE TO SUPPORT THE CLEAN WATER ACTION COMMITTEE EFFORTS TO RID OUR LOCAL WATER SUPPLY OF PERCHLORATE.

TONY FRANGELLO 618 S. ROYAL ST. ALEXANDRIA, VA 22314

Response: See response to comment code 6120.

Commenter Name: D.O. Luttz
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1864
EPA Comment ID: 20748
EPA Comment Code: 6120

Comment: 11/06/08

Dear EPA,

Please put a cap on perchlorates. Its polluting the and we don't need it.

D.O. Luttz 8004 Candlewood Dr. Alexandria, VA 22306

Response: See response to comment code 6120.

Commenter Name: Peter S. Toney
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1865
EPA Comment ID: 20749

EPA Comment Code: 6120

Comment: To the EPA

To whom it may concern:

I am a Virginia voter and am concerned about drinking water quality. Perchlorate is a dangerous chemical found in 37 states - we need to keep it out of our water supplies and it must be regulated.

Sincerely, Peter S. Toney

918 Green St. #1 Alexandria, VA 22314

Response: See response to comment code 6120.

Commenter Name: Jon
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1866
EPA Comment ID: 20750
EPA Comment Code: 6120

Comment: 11/06/08

Dear EPA,

You guys need to keep perchlorate out of my drinking water. I water to live!!!

Jon 6500 Hillview Ave. Alexandria, VA 22306

Response: See response to comment code 6120.

Commenter Name: Richard D. Weaver
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1867
EPA Comment ID: 20751
EPA Comment Code: 6120

Comment: Water Docket, EPA, Mailcode 2822T 1200 Pennsylvania Ave Washington, D.C. 20460 * ATTN: Docket ID No. EPA-HQ-OW-2008-0692

To whom it may concern,

I believe that the EPA should institute strict regulations on perchlorate in drinking water. I believe that there is strong evidence to suggest that it's presence in our drinking water is a significant risk to public health. There have not been sufficient routine tests on the effects of this chemical and it should be strongly regulated until such time as it is absolutely confirmed that it poses no significant health risk. Thank you.

Richard D. Weaver

Response: See response to comment code 6120.

Commenter Name: Robert S.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1869
EPA Comment ID: 20753
EPA Comment Code: 6120

Comment: 11/05/08

My drinking water

To Whom it May Concern @ the EPA. Please keep perchlorate out of my water: a nationwide primary drinking water regulation is needed to protect our public health. I support the clean water action.

Robert S. [Surname Illegible] 823 South Royal St Alexandria VA 22314

Response: See response to comment code 6120.

Commenter Name: Susan Willes
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1870
EPA Comment ID: 20754
EPA Comment Code: 6120

Comment: 11/07/08

Dear EPA,

I do not want perchlorate or harmful chemcial in our water

Susan Willes 110 Hume Ave Alex VA 22310 703-548-7762

Response: See response to comment code 6120.

Commenter Name: Janice Hollman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1871
EPA Comment ID: 20755
EPA Comment Code: 6120

Comment: OW-2008-0692

Attention EPA:

I, Janice Hollman, am concerned with the chemical, perchlorate, in our water system. Please use alternative chemcials in rocket fuel and explosives. It is very important.

Sincerely, J Hollman 319 Hume Ave Alexandria, VA 22301

Response: See response to comment code 6120. Regarding regulating use alternative rocket fuels, that is beyond the scope of this action.

Commenter Name: Norman Howard
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1872
EPA Comment ID: 20756
EPA Comment Code: 6120

Comment: Dear EPA,

I Norman Howard am very much apposed to harmful chemical and deposit in our water system.

Norman Howard 106 Hume Ave. Alex. VA 22301

Response: See response to comment code 6120.

Commenter Name: Margaret S. Guryan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1873
EPA Comment ID: 20757
EPA Comment Code: 6120

Comment: As a mother with an infant, I am very concerned about perchlorate in drinking water. Because of the harmful effects on children's development and fetuses, we need to limit this contamination in our drinking water. I urge the EPA to regulate this to keep our drinking water safe.

Margaret S. Guryan 221 E. Oxford Ave Alexandria VA 22301

Response: See response to comment code 6120.

Commenter Name: Meghan Hendy
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1874
EPA Comment ID: 20758
EPA Comment Code: 6120

Comment: November 5, 2008

Water Docket EPA Mailcode 2822T 1200 Pennsylvania Avenue Washington, DC 20460

ATTN: Docket ID No. EPA-HQ-OW-2008-0692

Dear Environmental Protection Agency:

I am very disappointed in your announcement to not regulate perchlorate in drinking water and respectfully ask you to reconsider this decision. Perchlorate has been proven to be a harmful chemical and can impair the thyroid gland, especially impacting fetuses and children. I urge you to establish a federal exposure standard.

Response: See response to comment code 6120.

Commenter Name: Meghan Hendy
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1874
EPA Comment ID: 20760
EPA Comment Code: 6120

Comment: As a mother of a toddler and a women in her childbearing years this is very concerning to me. We need a better federal tracking system for perchlorate and a higher exposure standard to protect our youngest citizens. Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought. It is imperative the the EPA implements a national primary drinking water regulation to protect public health.

Thank you for your consideration.

Sincerely, Meghan Hendy Alexandria, VA

Response: See response to comment code 6120.

Commenter Name: John Williams
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1875
EPA Comment ID: 20762
EPA Comment Code: 6120

Comment: I don't want perchlorate in may drinking water

John Williams 327 N. St. Asaph St. Alex., VA

Response: See response to comment code 6120.

Commenter Name: Sadea Ramsay
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1876
EPA Comment ID: 20763
EPA Comment Code: 6120

Comment: 11/7/08

To Whom it May Concern:

Perchlorate needs to be regulated by the EPA. Giving the federal government free reign to dump rocket fuel into our ground water is unacceptable. This is a huge threat to public health. This is a nationwide problem that needs to be addressed. Please put perchlorate contamination at the forefront of your drinking water regulations.

Thank you, SADEA RAMSAY 2406 CLYDE AVE APT #4 ALEXANDRIA, VA 22301

Response: See response to comment code 6120.

Commenter Name: Will Arttey
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1877
EPA Comment ID: 20764
EPA Comment Code: 6120

Comment: EPA water Docket,

I work as a chef in VA, and I vote I believe that perchlorate is a dangerous chemical, since It has been found in 37 states, Presents a wide spread threat to our health, It get into water supply so It must be regulated.

Sincerely Will Arttey 216 East Bellefonte Apt 1 Alexandria VA 22301

Response: See response to comment code 6120.

Commenter Name: Andrew E. Stevenson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1878
EPA Comment ID: 20765
EPA Comment Code: 6120

Comment: EPA Water Docket

Dear Regulators:

I am writing to express my support for increased federal regulation of perchlorate. It has serious health consequences - especially in young children; and shouldn't be given "a pass" as was recently done by the Bush Administration in its deal with the manufacturer.

Response: See response to comment code 6120.

Commenter Name: J. Sestak
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1879
EPA Comment ID: 20767
EPA Comment Code: 6120

Comment: We need a national policy for regulating perchlorate in our drinking water. This chemical is dangerous to our youth in particular due to it's harmful effects on the thyroid gland.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1883
EPA Comment ID: 20768
EPA Comment Code: 6120

Comment: I am outraged that EPA has not yet done its duty to protect the health of our families and communities from perchlorate pollution. This regulation must not be passed.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1886
EPA Comment ID: 20769
EPA Comment Code: 6120

Comment: regulate perchlorate now

Response: See response to comment code 6120.

Commenter Name: Tina Donze
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1887
EPA Comment ID: 20770
EPA Comment Code: 6120

Comment: Mr. Townsend,

As a concerned citizen and mother of two children, I am appalled at the fact that the EPA would allow a chemical such as perchlorate to be in our drinking water. There are enough chemicals in our drinking water and air that we should spend more time and money cleaning it up rather than deciding if we should allow current levels to stay as they are. I don't care if I have to pay more taxes to have regulations tightened on the amount of pollution and contaminants a company is allowed to release into our environment. We only have one planet and we are not doing enough to take care of it and it's people. Please make sure that my children and there children can grow up in a safe environment free from all the unnecessary chemicals. Thank you.

Sincerely, Tina Donze

Response: See response to comment code 6120.

Commenter Name: Rebecca Downey

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1888
EPA Comment ID: 20771
EPA Comment Code: 6120

Comment: Rebecca Downey 1211 Hazel St Charlottesville, VA 22902-4908

November 16, 2008

Administrator Stephen L. Johnson 1200 Pennsylvania Ave ., N .W. Rm. 1101A Washington, DC 20460

Administrator Johnson:

Dear Sir,

As a physician I am very concerned as to the EPA is considering not setting a federal drinking-water standard for perchlorate.

Response: See response to comment code 6120.

Commenter Name: M. Hoff
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1889
EPA Comment ID: 20775
EPA Comment Code: 6120

Comment: As a resident of northern New Mexico, in a region where high amounts of perchlorates have been found in certain water tables, especially those ajacent to Los Alamos National Laboratory, I strongly object to the EPA proposal not to regulate this poisonous substance. I realize the EPA has been seriously in decline during this current administration and systematically shedding responsibility left and right from protecting the American public from the depredations of out-of-control industries. But pretending a problem is not there will not make it go away. The EPA's shirking of responsibility makes it morally responsible for the health problems caused by its neglect. Please keep on regulating perchorates.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1890
EPA Comment ID: 20776
EPA Comment Code: 6120

Comment: Increasing the amount of pollution allowed in our drinking water has no positive benefits to the public, however, it has a great benefit to industy and big business. Money, money, money they cry, in their smoked filled rooms, pollution is the name fo the game and big business are

great at it. This rotten to the core president should be forced to drink the waters produced by big business manufacturing processes.

Response: This is not a comment, no response necessary.

Commenter Name: V. Foxx
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1892
EPA Comment ID: 20777
EPA Comment Code: 6120

Comment: This type of action further illustrates how little the government cares about the people they allegedly serve. The midnight rules are illustrative of carelessness, recklessness and a total lack of compassion. If I ever see George W. Bush in person, he WILL take the time to hear me out. If he is lucky, he'll still have all his teeth when we are done.

Response: No response necessary, this is not a comment.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1893
EPA Comment ID: 20778
EPA Comment Code: 6120

Comment: I am not really sure why in the world this one would even pass, other than the fact that someone is getting paid a lot of money. If we as the public have any say so if this one passes, I want to make it very clear that I appose this proposal. It's not safe, it is putting innocent lives in danger, and it is uncalled for. If this is Bush's way of getting back at America, well then all I can say is, God help him.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1894
EPA Comment ID: 20779
EPA Comment Code: 6120

Comment: I believe the safety of all people, especially children and pregnant women should be the first factor in deciding what contaminate levels are acceptable in drinking water. Bearing that in mind, I think all levels should be lowered never raised.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1895
EPA Comment ID: 20780

EPA Comment Code: 6120

Comment: Our drinking water must be strictly regulated. Perchlorate is known to be harmful to one's health. How are you supposed to feel safe if you know your water could potentially contain harmful chemicals? Please regulate our water, and protect our parks and environment. You are doing a wonderful job as I can see, please keep it up. We are all counting on you.

Response: See response to comment code 6120.

Commenter Name: Tim Cranford
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1896
EPA Comment ID: 20782
EPA Comment Code: 6120

Comment: The proposed relaxation of this standard is hazardous to the health and safety of millions of Americans. Rather than relaxing the standard, it would be much more advisable to decrease the "safe" levels of Perchlorate and bring them back down to the 2002 standard. Barring that, leave them as they are. None of us want to be drinking higher levels of this component of rocket fuel, nor do we want to be drinking higher levels of any other chemical. Drinking water in America should be clean. Anything less is unacceptable and puts the health of millions of Americans at risk. ~ Tim Cranford, US Citizen and Taxpayer

Response: See response to comment code 6120.

Commenter Name: Joe K.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1897
EPA Comment ID: 20783
EPA Comment Code: 6120

Comment: One begins to question his/her faith in our government when money becomes more important than the well-being of those who reside within it's rule. I believe the correct choise is obvious and hope that any other level minded person would agree.

~Joe K Redding, CA

Response: No response necessary, this is not a comment.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1902
EPA Comment ID: 20784
EPA Comment Code: 6120

Comment: I agree with Clean Water Action. I want my water clean!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1903
EPA Comment ID: 20785
EPA Comment Code: 6120

Comment: Please keep perchlorate out of our drinking water!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1904
EPA Comment ID: 20786
EPA Comment Code: 6120

Comment: Aren't there enough documented cases of health problems caused by contaminants in our water supply? Please do NOT allow perchlorate into our drinking water! Do your job and protect us!

Response: See response to comment code 6120.

Commenter Name: B. Pearlman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1907
EPA Comment ID: 20787
EPA Comment Code: 6120

Comment: Please regulate to make perchlorate levels very low in the drinking water. These chemicals can have adverse effects on the thyroid gland depressing it's function and causing obesity. We don't need more causes of obesity in this country.

Thank you.

Response: See response to comment code 6120.

Commenter Name: Amelia Kroeger
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1909
EPA Comment ID: 20788
EPA Comment Code: 6120

Comment: 6 November 2008

The U.S. Environmental Protection Agency should reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Perchlorate contamination is a nationwide problem and clearly has health impacts at lower levels than previously thought;

Give we citizens more serious consideration - a national primary drinking water regulation would help protect public health.

Thank you.

Amelia Kroeger 65 Stubbs Bay Road Maple Plain MN 55359

Response: See response to comment code 6120.

Commenter Name: Charlotte Morton
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1913
EPA Comment ID: 20789
EPA Comment Code: 6120

Comment: To whom it may concern,

I am writing to urge the regulation of Perchlorate in our drinking water. We should not have such chemicals in our water ignored. Please keep our water clean and safe.

Sincerely, Charlotte Morton

Response: See response to comment code 6120.

Commenter Name: Lucy Margolis
Commenter Organization: Educational Rights Advocates, Inc.
EPA Document ID: EPA-HQ-OW-2008-0692-1914
EPA Comment ID: 20790
EPA Comment Code: 6120

Comment: It is my understanding that the EPA has decided, as a preliminary decision, not to regulate perchlorate in drinking water. That being the case, I am writing to request that you reverse that decision. I REQUEST THAT YOU REGULATE PERCHLORATE IN DRINKING WATER.

It is my understanding that perchlorate is harmful to people - e.g., that it can impair the thyroid gland. As a person who has taken Rx Synthroid daily for many years, I personally support regulation of perchlorate so that others won't have impaired thyroid function.

It is my understanding that developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech, or deficits in motor skills. As an educational advocate for families of children with disabilities, I support regulation of perchlorate in order to reduce the potential number of children with special needs in the future.

It is my understanding that perchlorate has been found in at least 395 sites in 37 states, including 153 public water systems serving over 20 million people. That's a public health hazard that cannot be ignored. So, for these and other good and sufficient reasons, I REQUEST THAT YOU REGULATE PERCHLORATE IN DRINKING WATER.

Thank you for your time and consideration.

Regards,

Lucy Margolis, President Educational Rights Advocates, Inc. 10430 SW 99 Street Miami, Florida 33176 Phone (305) 279-8855 Fax (305) 279-4880 Cell (305) 588-3858 Lucyedu@aol.com

Response: See response to comment code 6120.

Commenter Name: Joshua Squire
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1917
EPA Comment ID: 20791
EPA Comment Code: 6120

Comment: I am greatly concerned about our exposure to toxic chemicals, both for environmental and personal health issues. Limiting our exposure can greatly increase our life-long health. Everything from household cleaners to beauty products and now to our drinking water seem to be loaded with toxins. The American people sometimes rely on government agencies to help protect it's constituents. It seems to me that if the EPA did not regulate a known toxin in our drinking water, then they would not be doing the service that they were organized for in the first place. I urge the EPA to regulate Perchlorate in our drinking water.

Thank you, Joshua Squire

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1918
EPA Comment ID: 20792
EPA Comment Code: 6120

Comment: I am quite diturbed that the EPA is considering NOT regulating perchlorate in the environment. It is the EPAs duty and should be morally obligated to do what is right for the health of the environment and citizens. Do not be pressured by other governement agencies or corporations and do what you were founded to do. Please...Do not risk the health of the environment and it citizens.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-1922
EPA Comment ID: 20794
EPA Comment Code: 6120

Comment: Please keep perchlorate out of my drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1923
EPA Comment ID: 20795
EPA Comment Code: 6120

Comment: I am appalled by the EPA's decision to NOT regulate perchlorate in drinking water. This is an astounding position for the agency to take since perchlorate can cause significant human health problems, even at levels much lower than previously thought. We and our children have enough insults to our health and immune systems each day without the EPA making it worse by working for corporations instead of the public at large. The EPA violates its fiduciary responsibility to the citizens of this nation by refusing to regulate a known toxin. Please reverse this decision. Please make the people in the EPA do their jobs. Protecting the public from these kinds of contaminants is what the agency exists to do. If the EPA does not step in and do what they were created for, then possibly it is time to do away with the EPA and replace it with an agency that will do its job.

Response: See response to comment code 6120.

Commenter Name: Robert L. Darwin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1926
EPA Comment ID: 20796
EPA Comment Code: 6120

Comment: The EPA should do whatever they can to keep Perchlorates out of our drinking water.

Robert L. Darwin Alexandria, VA 703-548-3595

Response: See response to comment code 6120.

Commenter Name: R. Perla
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1929
EPA Comment ID: 20797
EPA Comment Code: 6120

Comment: Please keep harmful toxins like perchlorate out of our drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1931
EPA Comment ID: 20798
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1932
EPA Comment ID: 20800
EPA Comment Code: 6120

Comment: Very simply, people shouldn't be forced to drink water that is toxic. Perchlorate in water can be measured. It's toxicity can be determined. Therefore limits on allowable amounts in drinking water can be drafted and enforced. Just do it!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1935
EPA Comment ID: 20801
EPA Comment Code: 6120

Comment: Please reconsider regulating perchlorate in drinking water. The health risks warrant it.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1938
EPA Comment ID: 20802
EPA Comment Code: 6120

Comment: You must develop an MCL for perchlorate, along with MTBE, TBA, and 1,4-dioxane, among others. It is totally irresponsible for EPA to cave to DOD, the petroleum industry and others and not protect the public. You work for US.

Get a move on with doing your job!

Response: Regarding regulating perchlorate in drinking water, see response to comment code 6120. Regarding regulating MTB, TBA and 1,4-dioxane, this is outside of the scope of this action.

Commenter Name: Yvonne Rost
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1946
EPA Comment ID: 20803
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. I don't want my children exposed to the effects of this chemical, nor would I want any family or friends to be afflicted by it.

Yvonne Rost Ferndale, MI

Response: See response to comment code 6120.

Commenter Name: J. Coleman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1948
EPA Comment ID: 20804
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. It's difficult to believe that a "protection" agency would accept a chemical that has health impacts at lower levels than previously thought. We should have a national drinking water regulation to provide a meaningful opportunity to protect public health

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1954
EPA Comment ID: 20805
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. When I learned that Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism, I was baffled by the EPA's even considering not to regulate it. It's used in rocket fuel and explosives and is a very harmful chemical. It should not be in drinking water, but even the EPA has found it in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher. Not setting a regulation for percholate is not environmental protection. I urge you, once again, to reverse your preliminary determination.

Response: See response to comment code 6120.

Commenter Name: Jay Lees
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-1957
EPA Comment ID: 20806
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water (Re: Document ID EPA-HQ-OW-2008-0692-0001). Perchlorate contamination has health impacts at lower levels than previously thought by experts. Additionally, developing and instituting a national primary drinking water regulation would provide a meaningful opportunity to protect public health. Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills. Our Governmental agencies should be in the business of passing regulations that help protect the health and livelihoods of all of the citizens of our great Country, and reversing the preliminary determination on Perchlorate contaminaltion levels in drinking water is one of many ways for a Government Agency to perform to its public charter. VR, Jay Lees, Lexington Park, Maryland.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1958
EPA Comment ID: 20807
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

* Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; * a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

This is COMPLETELY ridiculous! I cannot believe this is something that we have to be concerned about. In this country, in this time period, that I have to be worried about the water that I am drinking. You are the ENVIRONMENTAL PROTECTION AGENCY not the "let's make it easy for business to do whatever the hell they want" agency. PROTECT the environment and people! Honestly, what did you think you were supposed to be spending your time on when you applied at the EPA?

I'm seriously disturbed and disappointed.

Response: See response to comment code 6120.

Commenter Name:
Commenter Organization: The Night Move, LLC
EPA Document ID: EPA-HQ-OW-2008-0692-1960
EPA Comment ID: 20809
EPA Comment Code: 6120

Comment: Perchlorate contamination is a nationwide problem that can impact health at lower levels than previously thought. It is a dangerous chemical that affects the thyroid gland, potentially impairing the body's regulation of growth, development and metabolism. The EPA has found perchlorate in at least 153 public water systems. This chemical is used in rocket fuel and explosives. The companies creating these products with harmful side effects obviously aren't concerning themselves with the impact they are having on our environment. The government is allowing this. Ultimately, a regulation on the use of perchlorate would be the best answer to the health concerns of Americans. However, a national regulation of drinking water would also provide an opportunity to protect public health. Please, I urge the EPA to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Thank you.

The Night Move, LLC

Response: See response to comment code 6120.

Commenter Name: George Ferguson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1961
EPA Comment ID: 20810
EPA Comment Code: 6120

Comment: We have enough problems with the water quality now, please do not allow more problems by not regulating percholate in our water. There has to be a way of controlling water pollution.

Respectfully, George Ferguson

Response: See response to comment code 6120.

Commenter Name: Monica Juitt
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1963
EPA Comment ID: 20811
EPA Comment Code: 6120

Comment: Dear Official,

I am contacting you today to request the U.S. Environmental Protection Agency reconsider its preliminary determination to not set a regulation for perchlorate in drinking water. Perchlorate is a harmful chemical used in rocket fuel, flares, and explosives and even in small amounts can have very serious health impacts to our citizens. These include deficits in hearing, speech, motor skills and mental capacity.

Please look at the facts and consider regulating perchlorate in our drinking water.

Thank you,

Monica Juitt

Response: See response to comment code 6120.

Commenter Name: K. O'Sullivan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1965
EPA Comment ID: 20812
EPA Comment Code: 6120

Comment: Please do everything necessary to keep perchlorate out of our nation's drinking water.

Response: See response to comment code 6120.

Commenter Name: J. Nash
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1966
EPA Comment ID: 20813
EPA Comment Code: 6120

Comment: Your standards should be very tough regarding perchlorate and other contaminants in water. It is amazing to me that you would even consider removing perchlorate from your surveillance. This only reinforces what most already believe about Republicans, which is that you are in the service of one or another large business, not the public. Goodbye and good riddance in January!

Response: See response to comment code 6120.

Commenter Name: Ricarda G. Black
Commenter Organization: Welcome to Wellness
EPA Document ID: EPA-HQ-OW-2008-0692-1970
EPA Comment ID: 20814
EPA Comment Code: 6120

Comment: Please reverse your decision not to regular perchlorate.

Response: See response to comment code 6120.

Commenter Name: Barbara Sullivan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1976
EPA Comment ID: 20815
EPA Comment Code: 6120

Comment: Dear Sirs,

I always ask government agencies what their charge is. So, I wish to ask you what is your charge? Perchlorate is dangerous to human health and should thus be regualated. Government is to do for people what they cannot do for themselves. It is a great responsibility and yet a privilege to protect the people of this great nation. Not to regulate dangerous pollutants in our drinkng water seems like you have forgotten why this agency exists. Please answer your conscience when making decisions that impact our children.

Respectfull, Barbara Sullivan Citizen 2005 22nd Ave. NE Minneapolis, MN 55428

Response: See response to comment code 6120.

Commenter Name: Laurel
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1977
EPA Comment ID: 20816
EPA Comment Code: 6120

Comment: please keep our drinling water safe, no perchlorate

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1978
EPA Comment ID: 20817
EPA Comment Code: 6120

Comment: Please keep perchlorate out of drinking water, start regulating now.

Response: See response to comment code 6120.

Commenter Name: Dave Schaenzer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1979
EPA Comment ID: 20818
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

I do not want to drink perchlorate contamination in my water. This is a nationwide problem and has health impacts. I suggest that having a national primary drinking water regulation would provide a uniform standard that would protect public health at a federal level. This would save the cost of State by State regulations. This would also prevent long litigative process thru the individual states.

Thank You Dave Schaenzer

Response: See response to comment code 6120.

Commenter Name: D. Nelson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1981
EPA Comment ID: 20819
EPA Comment Code: 6120

Comment: Perchlorate must be regulated in drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1983
EPA Comment ID: 20822
EPA Comment Code: 6120

Comment: This chemical has been linked to thyroid problems in vulnerable populations of newborns, young children and pregnant women. The relaxation of this standard is harmful to public health.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1984
EPA Comment ID: 20823
EPA Comment Code: 6120

Comment: I would like to know how this is in some way justified by President Bush?? This is drinking water for the very same infants that Mr. Bush and company supposedly try to "save" from abortion. I guess once they are out of the womb, these babies are no longer politically important and can be given poison. Where are all the right wing evangelicals that are so angry about abortion but never say a word in protest of infants being provided poisoned water by our government?? What a conscience you must have Mr. Bush!! It is no wonder why you have been selected as one of the worst president's of our life time - I would say the worst in our entire history as a country. 27% approval rating?? do you have any shame? and to make matters worse, at the last minute of the presidency when people think you can't go any lower; you push forward with these insane laws! Amazing how selfish you can be. The days till your last day in office cannot come soon enough! Hope all your buddies with deep pockets are able to talk to your creator when its time for final judgement! Because from where I'm standing; you definitely have a long list of sins to account for!

Response: No response necessary, this is not a comment.

Commenter Name: Jasmin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1985
EPA Comment ID: 20824

EPA Comment Code: 6120

Comment: 11/06/08

Dear EPA,

I also do not want perchlorate in my drinking water.

Jasmin 326 N. Royal St. Alex. VA 22134

Response: See response to comment code 6120.

Commenter Name: Ben Spriggs
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1986
EPA Comment ID: 20825
EPA Comment Code: 6120

Comment: 11/06/08

Dear EPA,

Please cap perchlorate in my water resources.

Ben Spriggs 312 N. Royal St. Alexandria, VA 22134

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1991
EPA Comment ID: 20826
EPA Comment Code: 6120

Comment: Perchlorate needs to be reduced and or elimanted in the drinking water. This issue needs to be addressed and better regulated, not swept under the rug. This is a major health concern, and as a woman, mother and citizen of the USA, I am astounded that this issue with Perchlorate contaminating the water that I drink exist.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1992
EPA Comment ID: 20827
EPA Comment Code: 6120

Comment: Pushing through this regulation is harmful to the general populous and should not be continued until an acceptable review period has been established. This kind of government regulatory process without adequate review and study is unacceptable and only panders to special interest.

Response: EPA announced on October 10, 2008, its preliminary regulatory determination that a national primary drinking water regulation for perchlorate would not present "a meaningful opportunity for health risk reduction for persons served by public water systems." In response to requests from several stakeholders, EPA reopened the public comment period for an additional 15 days.

Commenter Name: T. Dginazio
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1993
EPA Comment ID: 20828
EPA Comment Code: 6120

Comment: I am outraged by this last minute rule changing. Will phone White House Monday to protest under cutting the public trust. The maximum safe level for perchlorate in drinking water is now 15 times higher than what was declared safe in 2002. Under this new standard, more than 16 million Americans are exposed to unsafe levels of perchlorate in their drinking water, and independent analysis shows anywhere from 20 to 40 million Americans at risk. Perchlorate has been found in the drinking water in 35 states in the U.S. This chemical has been linked to thyroid problems in vulnerable populations of newborns, young children and pregnant women. The relaxation of this standard is harmful to public health. outraged by this last minute rule changing.

Response: See response to comment code 6120.

Commenter Name: Aaron Peterson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1994
EPA Comment ID: 20829
EPA Comment Code: 6120

Comment: It has been shown that perchlorate greatly impacts human health by interfering with iodide uptake into the thyroid gland. Its greatest impact is on newborns, young children, and pregnant women. While small amounts of perchlorate may not pose a serious threat, large amounts endanger human health and water resources. A lack of regulation for perchlorate leaves me concerned for the developmental health of those most vulnerable to the chemical's effects.

-Aaron Peterson

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1995
EPA Comment ID: 20830

EPA Comment Code: 6120

Comment: Enough chemicals in our drinking water. The evidence from reports on the EPA's page show that perchlorate is toxic and we should not be drinking water with it. It is even found in mother's milk. The government is the cause of the contamination and the study was done by industry. It is obvious that the EPA is not really protecting the citizens. Regulate perchlorate.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1996
EPA Comment ID: 20831
EPA Comment Code: 6120

Comment: Regulate perchlorate now!

Response: See response to comment code 6120.

Commenter Name: Mary Moore
Commenter Organization: Lindon Park Neighborhood Association (LPNA)
EPA Document ID: EPA-HQ-OW-2008-0692-2002
EPA Comment ID: 20835
EPA Comment Code: 6120

Comment: EPA needs be moving toward the adoption of standards that protect the public from major health threats and not toward deregulation, especially when the primary exposure pathway for perchlorate is from contaminated drinking water.

Perchlorate is extremely persistent. Lack of regulation will not diminish this health risk to the public. LPNA respectfully requests that EPA develop a legal standard for perchlorate in drinking water.

Sincerely,

Mary Moore Lindon Park Neighborhood Association Phoenix, AZ

Response: See response to comment code 6120.

Commenter Name: Andy
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2006
EPA Comment ID: 20836
EPA Comment Code: 6120

Comment: Dear Sir or Madaam,

I think clean water is a good idea. Please do all you can to make sure it is clean.

Thanks Andy

Response: See response to comment code 6120.

Commenter Name: Heather Mastroddi
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2008
EPA Comment ID: 20838
EPA Comment Code: 6120

Comment: Water Docket ID # EPA-HQ-OW-2008-0692

To Whom It May Concern,

I would like to see more research on also regulating the harmful chemical perchlorate in our water.

Thank you,

Heather Mastroddi 601 Poplar St. Catasaqu, PA 18032

Response: See response to comment code 6120.

Commenter Name: Kimberly Scherman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2009
EPA Comment ID: 20842
EPA Comment Code: 6120

Comment: Docket ID # EPA-HQ-OW-2008-0692

To whom it may concern:

Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought. It can impair thyroid gland which controls growth, developmental health impairment. Please regulate this substance!!!!

Sincerly,

Kimberly Scherman 640 S. 14th St. Catasaqua, PA 18032

Response: See response to comment code 6120.

Commenter Name: Brenda Heininger
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2013
EPA Comment ID: 20845
EPA Comment Code: 6120

Comment: I feel primary drinking water regulation is needed to protect public health.

Perchlorate is a very harmful chemical which needs to be regulated.

Brenda Heininger 2317 Silo Dr. Easton, PA 18040

11/10/08

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2014
EPA Comment ID: 20847
EPA Comment Code: 6120

Comment: What could the EPA possibly be thinking? PLEASE, PLEASE.....regulate this chemical in our drinking water!!!!!

Response: See response to comment code 6120.

Commenter Name: E. Cuffari
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2015
EPA Comment ID: 20848
EPA Comment Code: 6120

Comment: Please reverse this decision on the regulation of Perchlorate in our drinking water. The last thing we need is Another chemical doing harm to US and our children. Since this chemical has been found in 37 states drinking water , I feel it's important to regulate.

Response: See response to comment code 6120.

Commenter Name: Lynn Thorp
Commenter Organization: Clean Water Action
EPA Document ID: EPA-HQ-OW-2008-0692-2017
EPA Comment ID: 20850
EPA Comment Code: 6120

Comment: Clean Water Action has been concerned about perchlorate contamination for many years and has worked with communities facing perchlorate contamination of their water supplies and in several states where drinking water standards have been considered and/or set. Drinking water is a priority area for the organization and we work on many aspects of Safe Drinking Water Act implementation.

Clean Water Action urges the Agency to reconsider its preliminary determination NOT to set a Maximum Contaminant Level (MCL) for perchlorate at this time. With tens of millions of drinking

water consumers affected and given that perchlorate affects some of our most vulnerable people the most - infants and children - there is a meaningful opportunity for health risk reduction.

Response: See response to comment code 6120.

Commenter Name: Donna Wolsted
Commenter Organization: Gleason Lake Improvement Association (GLIA)
EPA Document ID: EPA-HQ-OW-2008-0692-2018
EPA Comment ID: 20852
EPA Comment Code: 6120

Comment: We want to maintain the best drinking water we can.

Please eliminate percholate from rocket fuels and explosives.

We have to be aware that the cancer and other diseases in U.S. have some strong contributing factors that other countries do not have.

I am not willing to risk my health on having more chemicals in our food or water. because the gov. "thinks" it is safe. Donna Wolsted, GLIA

Response: See response to comment code 6120.

Commenter Name: Lenny Siegel
Commenter Organization: Center for Public Environmental Oversight
EPA Document ID: EPA-HQ-OW-2008-0692-2019
EPA Comment ID: 20856
EPA Comment Code: 6120

Comment: If EPA were serious about protecting the health of America's children, it would move forward with plans to develop a legal standard for perchlorate in drinking water. In the course of that effort, it should consider how other contaminants might contribute to the problem.

Finally, over the past decade, our understanding of the perchlorate threat has changed. Large sources of perchlorate pollution, associated with rocket-fuel production and other industrial activity, remain. However, it appears that perchlorate exposure is widespread at low levels also because of natural, agricultural, and incidental sources. To develop a public health strategy that addresses such exposures, we need a drinking water standard that requires the sampling of our water supplies at the low levels found to be a potential problem by the Centers for Disease Control. Even if it turns out that other factors-such as low iodine consumption-play a key role in the manifestation of thyroid dysfunction, such sampling is essential to protect the health of our children for decades to come.

Sincerely, (submitted electronically) Lenny Siegel Executive Director

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-2022
EPA Comment ID: 20857
EPA Comment Code: 6120

Comment: It doesn't take a rocket scientist to know that drinking rocket fuel is unhealthy. Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. Is there any question that Perchlorate in our water needs to be banned?

Response: See response to comment code 6120.

Commenter Name: Doug Bendele
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2025
EPA Comment ID: 20858
EPA Comment Code: 6120

Comment: I urge the EPA to regulate perchlorate in drinking water. Perchlorate contamination has been found to be a nationwide problem with potentially devastating medical effects. Please exercise the authority given to you to protect my children and yours.

Doug Bendele, human, father, husband, citizen, engineer

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2026
EPA Comment ID: 20859
EPA Comment Code: 6120

Comment: NO perchlorate in my water please regulate, accountability good - clean water best.

Response: See response to comment code 6120.

Commenter Name: E.D. Levinson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2036
EPA Comment ID: 20860
EPA Comment Code: 6120

Comment: It seems more than dangerous NOT to regulate perchlorate - please reconsider immediately.

Thank you.

Response: See response to comment code 6120.

Commenter Name: Hannah Durocher
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2037
EPA Comment ID: 20861
EPA Comment Code: 6120

Comment: As a member of the general public, I was horrified to hear that the EPA is considering NOT regulating perchlorate in drinking water. This chemical has been shown to be harmful to human and animal health.

As someone with a thyroid problem who has seen the number of people with thyroid problems increase over the last few decades, I was appalled to learn that the EPA has made a preliminary decision to not regulate a substance that has been shown to damage the thyroid gland.

In our time of bottled spring water for the wealthy, the failure to regulate perchlorate would disproportionately affect the health of the middle class and working poor. This is immoral and bad for health care costs.

The purpose of the government is to serve the needs of the people--not the needs of industry without any consideration for the people. I urge the I urge the EPA to reverse its preliminary decision and make a stand for moral stewardship of our nation's drinking water.

Hannah Durocher 1407 N. Kenilworth St. Apt. 3 Arlington, VA 22205

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2038
EPA Comment ID: 20862
EPA Comment Code: 6120

Comment: Dear EPA:

Please regulate the percholate in drinking water and protect public health. I understand the contaminant can have harmful affects at levels lower than thought previously.

Thank you for your attention to this matter.

Response: See response to comment code 6120.

Commenter Name: M. King
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2041
EPA Comment ID: 20863
EPA Comment Code: 6120

Comment: You must regulate Perchlerate in Drinking water, We do not know the possible effects that ingestion of this toxic chemical can cause. Start Regulating it Now!

Response: See response to comment code 6120.

Commenter Name: R. James
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2044
EPA Comment ID: 20864
EPA Comment Code: 6120

Comment: Keep Perchlorate out of our Drinking Water.

Response: See response to comment code 6120.

Commenter Name: Gabriel Donovan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2046
EPA Comment ID: 20865
EPA Comment Code: 6120

Comment: To the EPA,

I write to petition for the regulation of Perchlorate in America's water resources. As with all chemical ingredients in use today, Perchlorate is a mystery. A mystery in that we do not know the long term ramifications of exposure in humans and to the environment. The preliminary findings point to ill effects in both regards. For this reason I strongly urge you to reconsider your position of non regulation. We the people of the United States depend on your vigilant watch to protect us from the danger of industrial pollutants. Regulate Perchlorate.

Sincerely,

Gabriel Donovan Texas

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2047
EPA Comment ID: 20866
EPA Comment Code: 6120

Comment: Our healthcare system needs reform and Social Security is straining and will get worse. The health problems brought on by not regulating percolate can be prevented. It is irresponsible to ignore this element and deem it as harmful.

Please reverse your decision.

Response: See response to comment code 6120.

Commenter Name: Kathryn S Taylor
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2048
EPA Comment ID: 20867
EPA Comment Code: 6120

Comment: Please, please, please reconsider this decision to allow perchlorate in our drinking water. We are facing enough cancer and other health issues because of chemicals in our water and soil.

For health, Kathryn S Taylor 154 SE Lincoln Circle North St. Petersburg, FL 33703

Response: See response to comment code 6120.

Commenter Name: Della R. Post
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2053
EPA Comment ID: 20868
EPA Comment Code: 6120

Comment: I am appealing to you in the interest of all citizens who drink water (everyone, including you) to reverse your decision not to regulate the amount of Perchlorate in our water supplies. Too many studies have found clear danger allowing this contaminent to remain in our water. To allow it to continue harming us is irresponsible behavior from an organization whose job is to protect the American people.

Sincerely, Della R. Post 154 Village Circle Oakdale, PA 15071

Response: See response to comment code 6120.

Commenter Name: Justin White
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2058
EPA Comment ID: 20869
EPA Comment Code: 6120

Comment: Can anyone come up with one good reason to put Perchlorate in the drinking water? Aside from the obvious one, which is that it is the cheapest, and sneakiest, way for a corporation/government to get rid of a dangerous byproduct. As was done with fluoride, a byproduct of aluminum smelting, and ammonium, which killed all of my fish and thus, can't be all that good for you.

Adding Perchlorate to our drinking water is a ridiculous notion and everyone knows it. Wouldn't it be nice if people were truthful and responsible and took accountability for their actions?

Concerned Citizen, Justin White

Response: Perchlorate is not added to drinking water. There are three principal sources of the perchlorate in the environment: its use as an oxidizer (rocket propellants, fireworks, flares and explosives), its presence in Chilean nitrate fertilizer, and formation via atmospheric processes.

Commenter Name: Margaret Tait
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2062
EPA Comment ID: 20870
EPA Comment Code: 6120

Comment: I have lived with thyroid disease for 13 years. It makes every day harder and has effected every aspect of my health and life. Without regulation, sadly, industry does not often take the action needed to protect the public from contaminants. It makes no sense to accept any risk to our children's health. We must regulate perchlorate's presence in our water.

Margaret Tait Brighton, Michigan

Response: See response to comment code 6120.

Commenter Name: Pamela Rogow
Commenter Organization: Eco Impresario Services
EPA Document ID: EPA-HQ-OW-2008-0692-2063
EPA Comment ID: 20871
EPA Comment Code: 6120

Comment: News of the EPA's impending reversal of its initial determination to protect drinking water from perchlorate contamination is a great mistakes. Please protect the public from this danger.

Response: See response to comment code 6120.

Commenter Name: Susie Bryan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2065
EPA Comment ID: 20872
EPA Comment Code: 6120

Comment: Please do not contaminate the water with one more chemical. We have a daughter affected with autism and is not able to detoxify herself very well due to low glutathione levels. This is common with children affected by autism. Whether or not the EPA finds that there is a safe amount that does not cause long-term affects on "people" doesn't speak to the large population of people that are having a hard time processing all the chemicals that are CURRENTLY out there.

Please hear our voices and don't add any more chemicals to the water that do (in some part) have a toxicity level (even though they haven't shown to have a large effect). Any toxicity is a lot of toxicity for a child on the spectrum!

Susie Bryan

Response: Perchlorate is not added to drinking water. There are three principal sources of the perchlorate in the environment: its use as an oxidizer (rocket propellants, fireworks, flares and explosives), its presence in Chilean nitrate fertilizer, and formation via atmospheric processes.

Commenter Name: J. and D. Dietz
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2066
EPA Comment ID: 20873
EPA Comment Code: 6120

Comment: Pls. do not allow rocket fuel to remain in our water. You may say it is not harmful but what is causing our sicknesses and cancers? Water should be clean and have no man made or natural substances in it which could cause harm. Who knows what we will find out in the future concerning our digesting rocket fuel. This is preposterous!! Filter it out of our water!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2068
EPA Comment ID: 20874
EPA Comment Code: 6120

Comment: We need cleaner water. Please protect us from chemicals like perchlorate!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2069
EPA Comment ID: 20875
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Donna Levin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2070
EPA Comment ID: 20876
EPA Comment Code: 6120

Comment: Please change your decision on percholate, and regulate its presence in drinking water. We depend on you. Thank you.

Donna Levin Elkins Park, Pennsylvania

Response: See response to comment code 6120.

Commenter Name: Susan S. Merrill
Commenter Organization: Clean Water Action
EPA Document ID: EPA-HQ-OW-2008-0692-2073
EPA Comment ID: 20877
EPA Comment Code: 6120

Comment: Greetings:

Please reverse the deregulation of perchlorate, a chemical found in rocket fuel, from drinking water in the United States. Americans need clean drinking water and should be protected from contaminants in it such as perchlorate.

Thank you for making this change in the law.

Sincerely,

Susan S. Merrill Member, Clean Water Action

Response: See response to comment code 6120.

Commenter Name: Caryn Mandelbaum
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2076
EPA Comment ID: 20878
EPA Comment Code: 6120

Comment: Why bother having an EPA when it is unwilling to carry out its purpose-- to secure clean water (all water), air and land? Specifically, by denying its responsibility to regulate perchlorate in drinking water, the EPA is offending the leaders that chartered the institution and all people affected by its irresponsibility.

Perchlorate contamination is a problem nationwide. A small amount of this pernicious chemical poses a massive threat to our freshwater resources-- groundwater. There are communities, like some near me in California, that are nearly entirely dependent on groundwater. They can only expect to suffer grave health impacts from drinking perchlorate-laden groundwater. All the EPA has done here is to declare a Superfund site. That is unacceptable.

The EPA was created in order to be responsible for the government and government-sanctioned industrial pollution to our natural resources. Perchlorate found its way into our drinking water supply as a result of the Department of Defenses contracts with the aerospace industry. It sounds like paranoia, but I know the industry's and government's protective measures or accountability could not be further from the truth.

If you are not going to stand up to your responsibility, stop wasting my tax dollars and get out of a regulatory regime. If you are going to continue to pretend to be the department that secures clean water, air and land, then set perchlorate standards and clean-up superfund sites.

By all means, I expect a response-- both national and personal.

Sincerely, Caryn Mandelbaum, carynm5@gmail.com

Response: Regarding regulating perchlorate, see response to comment code 6120. Regarding cleaning up Superfund sites, see response to comment code 6300.

Commenter Name: Theresa Quigley-Uhl
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2077
EPA Comment ID: 20879
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. Please keep our water free from harmful chemicals. Keep our children healthy.

Thank you, Theresa Quigley-Uhl 1134 Snyder avenue philadelphia,PA 19148

tajuhl7@aol.com

Response: See response to comment code 6120.

Commenter Name: Robin Porter
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2078
EPA Comment ID: 20880
EPA Comment Code: 6120

Comment: I urge the EPA to reconsider its regulation of perchlorate in our drinking water. This chemical can cause serious health issues in developing fetuses and children, and it's long-term effects are not known. We shouldn't risk the lives of our children to find out! Please keep our drinking water clean, safe and free of harmful chemicals such as perchlorate.

Thank you, Robin Porter Concerned citizen

Response: See response to comment code 6120.

Commenter Name: Michael Doxy
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2079
EPA Comment ID: 20881
EPA Comment Code: 6120

Comment: 11/5

To Whom it May Conern

I would like to support the Clean Water Action Committees efforts to rid our local water supply of perchlorates.

Michael Doxy 706 S. Royal St Alexandria, VA 22314

Response: See response to comment code 6120.

Commenter Name: Teresa Jordan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2080
EPA Comment ID: 20882
EPA Comment Code: 6120

Comment: 3152 Shad Court Simi Valley, CA 93063 November 26, 2008

Water Docket US EPA Mailcode: 2822T 1200 Pennsylvania Avenue, N.W. Washington, DC 20460

Re: DOCKET ID No. EPA-HQ-OW-2008-0692 (Preliminary Regulatory Determination on Perchlorate--Reopening of Public Comment Period (November 28, 2008 Deadline)).

Dear Mr. Grumbles, and Mr. Burneson:

I just read through the Santa Susana Field Laboratory's Perchlorate Work Plan, the State Water Resources Control Board's Proposed Recycled Water Policy Staff Report, and after mulling through my recent letters addressing the State Water Resources Control Board's proposed review of California's Anti-Degradation Policy (Resolution 68-16), I am convinced more than ever that it is of the utmost importance the USBPA initiates development of a national regulation for perchlorate in drinking water ASAP because if the types of decisions on water quality issues made by California's State and Regional Water Quality Control Boards are indicative of trends in the other 49 States such state of affairs significantly impact Americans nationwide.

Sincerely, Mrs. Teresa Jordan

Enclosures:

November 19, 2008, Letter to the State Water Resources Control Board; Anti- degradation Policy. (3 Pages) [See PDF Docket ID EPA-HQ-OW-2008-0692-2080]

November 20, 2008, Letter to the State Water Resources Control Board; Anti- degradation Policy. (5 Pages) [See PDF Docket ID EPA-HQ-OW-2008-0692-2080]

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #8 - Food and Water Watch

EPA Document ID: EPA-HQ-OW-2008-0692-1805
EPA Comment ID: 20883
EPA Comment Code: 6120

Comment: Dear Administrator Johnson,

I am writing to urge you to reconsider EPA's preliminary determination not to regulate perchlorate in drinking water.

Perchlorate has been found in the drinking water supply of 35 states and the District of Columbia. Widespread human exposure to perchlorate was confirmed by the Center for Disease Control's NHANES study, which found that 100 percent of the 2,820 randomly selected study participants had detectable levels of perchlorate in their urine.

The widespread exposure of the population to some level of perchlorate raises serious health concerns. Perchlorate can inhibit the thyroid gland's iodine uptake, potentially leading to hypothyroidism. Severe hypothyroidism during pregnancy can lead to abnormal fetal cognitive development, and even mild hypothyroidism during pregnancy is associated with subtle cognitive defects in children. Thus, perchlorate could alter fetal brain development, having lifelong cognitive effects for those affected.

EPA's failure to regulate perchlorate in drinking water places consumers - especially children and pregnant women - at risk.

In response to this misguided determination, EPA's own Children's Health Protection Advisory Committee has drafted a letter expressing its concern with EPA's decision not to regulate perchlorate. Members of the committee claim that EPA rushed a decision on perchlorate without taking time to consider all the latest peer-reviewed studies.

Given the vital importance of fetal central nervous development not only for long-term health and development of children, but also for the viability of fetuses, why would EPA rush to a decision? Unfortunately, the only conclusion we can draw is that EPA has issued this determination to avoid strapping the Department of Defense with costs to clean up near military bases, missile testing sites and chemical plants. While millions of consumers' health is jeopardized, it seems the budget concerns of the Pentagon or White House are driving EPA's decision.

This determination is clearly another instance of a regulatory agency shirking its responsibility to protect the American public. Instead of fulfilling its obligations under the SDWA, EPA has once again folded to pressure.

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #6 - Earth Justice
EPA Document ID: EPA-HQ-OW-2008-0692-0972
EPA Comment ID: 20884
EPA Comment Code: 6120

Comment: Administrator Stephen L. Johnson 1101A EPA Headquarters 1200 Pennsylvania Avenue, NW, Ariel Rios Building Washington, DC 20460

Subject: Protect Our Drinking Water From Perchlorate Contamination

Dear Administrator Johnson,

I am writing to urge you reverse EPA's preliminary regulatory determination and set a protective drinking water standard for perchlorate as required by the Safe Drinking Water Act.

Perchlorate contamination in our food and water supplies is too widespread, and its toxic effects too well known, for continued inaction on this problem.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1799
EPA Comment ID: 20887
EPA Comment Code: 6120

Comment: I cannot believe that this is something that is even being debated. The idea of allowing an ingredient that is in rocket fuel to even be present in any percentage in our drinking water is utterly ridiculous.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1884
EPA Comment ID: 20888
EPA Comment Code: 6120

Comment: This is crazy. Why would this administration go against the SCIENCE of this action? Are you trying to scheme your way into making the public FEAR tap water in order to boost the sales of bottled water by your best friends and corporate companies while putting the public health at risk? Wow, so there is actually movements being created around the support of tap water and against corporate giants. You're afraid of the people getting this right. Do the right thing in your last days in office. I really fear for the world you are leaving your children. Does that EVER cross your mind? Greed never solved any problems in our country. Grow up.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1891
EPA Comment ID: 20889
EPA Comment Code: 6120

Comment: For Bush to pass something as absurd as this is pretty low of him. I would expect this out of a Republican, however. Most Republicans are only out for themselves or others who can provide top dollar. Perchlorate keep increasing in the drinking water. What will happen when they increas again? Will there be another determination of how safe the water is? Will the water still be declared 'safe'? I bet that if Bush and the rest of his administration had to drink the water, they would not pass such a thing. When will there be anyone in any sort of political office/setting who will care about the average American? Congress and the rest of capital know this, I am sure, but if the average American were to stand up and not take any of the [expletive] that was being fed to us, the people would actually be able to take charge of this country like it should be. The United States is becoming a [expletive] due to things (this docket) like this, and is alos why China is the next 'Land of Opportunity'. The U.S.A. is now the 'Land of Degregation and No Hope'.

Thanks for the terrible job everyone on Capital Hill. I hope you enjoy destroying this once great country.

Response: No response necessary, this is not a comment.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1921
EPA Comment ID: 20890
EPA Comment Code: 6120

Comment: Someone better change the regulations on what is acceptable. 0% There is enough crap in the drinking water that EPA say is acceptable. Is it acceptable to POISON us? Let's regulate something that matters. I don't care if it's PPM or PPB the perchlorate levels are still unacceptable.

Response: See response to comment code 6120.

Commenter Name: D'Lanie Blaze
Commenter Organization: TheAeroSpace
EPA Document ID: EPA-HQ-OW-2008-0692-0641
EPA Comment ID: 20891
EPA Comment Code: 6120

Comment: To Whom It May Concern:

I am very concerned that the EPA is poised to walk away from monitoring perchlorate in our drinking water. Given the documented risk this contaminant poses to public health, this decision contradicts the purpose for which this agency was designed.

Southern California's main industries during the 1950's and 1960's were atomic energy and aerospace. Santa Susana Field Laboratory (SSFL) was home to over 30,000 rocket engine tests and the worst nuclear accident in US history. During the Cold War and Space Race, the Atomic Energy Commission (AEC) and Department of Energy (DOE) encouraged rampant environmental pollution in the name of production and experimentation, resulting in massive contamination to ground and surface water. Presently, SSFL languishes in a state of contamination. Perchlorate

remains a concern within our community; it has repeatedly tested beyond "safe" levels in drinking water, and thyroid issues are staggering in the neighborhoods surrounding SSFL. This is a nationwide concern, especially in communities that border military bases with a history of missile development.

The DOE continues to evade accountability for environmental crimes, which spanned decades. The EPA's cavalier approach to public safety regarding perchlorate sets a dangerous precedent.

Predictably, the public has been inadequately informed and provided with little time to offer educated comment before the opportunity to take part in the decision-making process expires. The EPA's attempt to rush this decision before administrative change - and while meeting only the minimum requirements for public participation (which are inept at best) - is very telling. The decision to cease monitoring for perchlorate in drinking water likely augurs trouble on the horizon for our citizens, the majority of which blindly trust agencies like the EPA to fulfill their responsibilities in an ethical, if not logical, fashion.

Sadly, the opportunity to access information and become involved in decisions like this one are difficult. Conversely, the public is bombarded with pharmaceutical ads which announce the availability of a wide variety of medication which is arguably necessary as a result of our routine exposure to a variety of toxins and pathways. Thyroid issues are steadily rising, and yet the government body tasked with this issue is willing to walk away from it. This does nothing but give rise to the possibility of collusion between EPA and pharmaceutical corporations. What is the pay-off for walking away from perchlorate? This is certainly not a decision motivated by commitment to public safety.

Response: See response to comment code 6120.

Commenter Name: Brie Brigham
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1436
EPA Comment ID: 20893
EPA Comment Code: 6120

Comment: Brie Brigham 118 South Gill Street State College, PA 16801 October 29, 2008

Office of Ground Water and Drinking Water (4601) Ariel Rios Building 1200 Pennsylvania Avenue, NW Washington, DC 20460-0003

To Whom It May Concern,

I support the EPA's decision to regulate the concentration in drinking water, but believe the perchlorate contamination level considered safe should be lowered. Perchlorate occurs both naturally and through manufacturing, and is found in rocket fuel, fireworks, and airbags. Perchlorate enters United States drinking water from improper disposal by test sites, military bases, and chemical plants. A 2005 report by the EPA stated that the chemical compound polluted soil, groundwater, and drinking water in 35 states and has contaminated 153 public water systems in 26 states. The report also estimated that 16.6 million Americans are exposed to perchlorate at levels scientists

consider unsafe. Perchlorate contamination in drinking water can have devastating effects, particularly on fetuses, newborns, and children.

Response: See umbrella response under 6120.

Commenter Name: Brie Brigham
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1436
EPA Comment ID: 20896
EPA Comment Code: 6120

Comment: In conclusion, I applaud the EPA's decision to regulate perchlorate concentrations in drinking water. However, I believe the contamination level should be lowered so that fetuses, newborns, and children are not exposed to levels that are unsafe.

Sincerely, Brie Brigham

Response: Please see the response to comment code 6120.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20898
EPA Comment Code: 6120

Comment: EPA's Preliminary Regulatory Determination on Perchlorate is an embarrassment to the agency. It marks the next step in a long journey away from sound science, impartiality, and public health protection towards biased decisions where the agency no longer even attempts to hide its partiality towards industry interests.

Response: This is not a comment, a response is not necessary.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20902
EPA Comment Code: 6120

Comment: The combined effect of these multiple layers of corruption has been to make perchlorate look safe when it is not, and to make EPA appear as though it is simply servicing perchlorate polluters, which it is. The agency's proposed action is nothing less than pandering to perchlorate polluters who would be made to clean up the tap water of 40 million people in 27 states if the agency were to conduct an honest assessment of the human health risks of perchlorate.

This assessment makes a mockery of everything EPA stands for. It must not be adopted.

Response: See response to comment code 6120.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20908
EPA Comment Code: 6120

Comment: The scientific evidence clearly points to the need for EPA to set a health protective drinking water standard for perchlorate - that is, a standard lower than the level shown to be associated with altered thyroid hormone levels in American women with low iodine intake. Unfortunately, EPA has relied on questionable science, an even more questionable computer model, and circular logic to justify its proposal to not regulate this harmful contaminant at all in our nation's drinking water. This is inexcusable.

EWG urges EPA to overhaul its poorly crafted assessment according to the points described in detail below and to live up to its mandate of protecting public health by setting a stringent drinking water standard for perchlorate.

Response: See response to comment code 6120.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20917
EPA Comment Code: 6120

Comment: Conclusion

As outlined above, EPA's preliminary regulatory determination on perchlorate is rife with errors, omissions, and wrong assumptions. EPA relies on a computer model that was generated using the now discredited Greer study. In addition, EPA chooses to ignore the valuable data from human studies like the Blount study that show potential health risks to millions of U.S. residents from perchlorate exposures much lower that the proposed HRL of 15 ppb. EPA also disregards the vulnerability of breast fed infants and young children, in whom current perchlorate exposures could potentially result in decreases in thyroid hormone levels that have long-term adverse effects on brain development and growth. Perhaps most egregious is EPA's finding that protecting 30,000 pregnancies annually is not a sufficient reason to regulate this dangerous contaminant in drinking water.

Response: See response to comment code 6120.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group
EPA Document ID: EPA-HQ-OW-2008-0692-1432
EPA Comment ID: 20919
EPA Comment Code: 6120

Comment: In the meantime, EWG calls on EPA to fix the numerous glaring errors in its assessment and to quickly move to set a health protective drinking water standard for perchlorate.

Sincerely,

Dr. Anila Jacob, MD, MPH Senior Scientist Environmental Working Group

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Pearce EN, Leung AM, Blount BC, Bazrafshan HR, He X, Valentin-Blasini L, Braverman LE. 2007. Breast Milk Iodine and Perchlorate concentrations in Lactating Boston Area Women. Journal of Clinical Endocrinology and Metabolism 92(5):1673-7

Response: See response to comment code 6120.

Commenter Name: Lucy Allen
Commenter Organization: Pacific Institute
EPA Document ID: EPA-HQ-OW-2008-0692-1770
EPA Comment ID: 20925
EPA Comment Code: 6120

Comment: November 5, 2008

Administrator Stephen L. Johnson Water Docket, Environmental Protection Agency 2822T, 1200 Pennsylvania Ave., NW Washington, D.C. 20460

RE: Drinking Water: Preliminary Regulatory Determination on Perchlorate, Federal Register October 10, 2008, (73 FR 60262) (FRL-8727-6) Docket Number: EPA-HQ- OW-2008-0692

Dear Mr. Stephen Johnson,

The Pacific Institute would like to formally submit the following comments on the Environmental Protection Agency's (EPA) Drinking Water Preliminary Regulatory Determination on Perchlorate. After reviewing the Preliminary Determination and relevant literature, we do not agree with the EPA's determination that regulating perchlorate presents no "meaningful opportunity for health risk reduction for persons served by public water systems." While we recognize that the science upon which the determination is based has been contested, our comments address a number of further concerns, including the protection of vulnerable populations; the impacts that the determination will have on remediation efforts and future monitoring; and the criteria for what is considered to be a "meaningful opportunity" for protection of public health.

Response: This is not a comment, a response is not necessary.

Commenter Name: Lucy Allen
Commenter Organization: Pacific Institute
EPA Document ID: EPA-HQ-OW-2008-0692-1770
EPA Comment ID: 20928
EPA Comment Code: 6120

Comment: Ongoing monitoring of drinking water is needed to safeguard public health. The EPA's preliminary decision to not regulate perchlorate was contingent on the fact that a relatively small number of public water systems currently contain levels of perchlorate at unsafe levels. While this

may be true today, it may change, as perchlorate is widely used and easily leached. With uncertainties surrounding the extent of current contamination, and continued use of perchlorate,[FN11: Both Trumpolt et al. and Aziz et al. identify uncertainties in how current uses of perchlorate, e.g. in road flares and fireworks affect groundwater perchlorate levels. See footnotes 12,13.] the EPA should set a Primary Drinking Water Regulation to make ongoing monitoring mandatory.

According to GAO 2007, federal and state agencies have found perchlorate in groundwater, surface water, soil, or public drinking water systems at almost 400 sites in 37 states, in concentrations ranging from 4 ppb to more than 3.7 million ppb. The GAO contends that "it is difficult to determine the extent of perchlorate in the United States or the status of any cleanup actions because EPA does not centrally track or monitor perchlorate detections, environmental releases, or cleanup activities."

Many potential sources of perchlorate contamination in the U.S. exist, including munitions manufacture and disposal, use of explosives in rock blasting, manufacture and use of fireworks, manufacture and use of safety flares, and use of Chilean nitrate fertilizers.[FN12: Trumpolt, C., M. Crain, G. Cullison, S. Flanagan, L. Siegel, and S. Lathrop. (2005). Perchlorate: Sources, Uses, and Occurrences in the Environment. Retrieved Oct 27, 2008 from http://yosemite.epa.gov/r10/CLEANUP.NSF/PH/Arkema+Technical+Documents/$FILE/Perchlorate-Sources-Occurance-In-The-Environment.pdf.],[FN13: Aziz, C., R. Borch, P. Nicholson, and E. Cox. (2006). Alternative Causes of Wide-Spread, Low Concentration Perchlorate Impacts to Groundwater. GeoSyntec Consultants, Guelph, ON, Canada. Retrieved Oct 27, 2008 from http://www.springerlink.com/content/p8m017624280752w/.] In addition to these ongoing uses of perchlorate, there may be environmental contamination from historic releases, for example from manufacture and disposal. This widespread use is likely to lead to further water contamination, as perchlorate is readily leached from soil into groundwater due to its high solubility and persistence in the environment.

Response: See response to comment code 6120.

Commenter Name: Lucy Allen
Commenter Organization: Pacific Institute
EPA Document ID: EPA-HQ-OW-2008-0692-1770
EPA Comment ID: 20929
EPA Comment Code: 6120

Comment: The EPA determined that regulating perchlorate in drinking water does not pose a meaningful opportunity to protect public health-even as its report recognizes that 900,000 people will remain exposed to perchlorate at levels that could exceed the health reference level, up to 30,000 of which are pregnant women at any given time. Protecting the health of these individuals, even if it is a small group, is significant, and the federal government has the capacity and responsibility to do so.

Response: See response to comment code 6120.

Commenter Name: Ron Curry
Commenter Organization: New Mexico Environment Department
EPA Document ID: EPA-HQ-OW-2008-0692-1796

EPA Comment ID: 20931
EPA Comment Code: 6120

Comment: In its preliminary determination, EPA has tentatively decided not to promulgate maximum contaminant levels (MCL's) for perchlorate under the federal Safe Drinking Water Act (SDWA), 42 U.S.C. [sections] 300f to 300j-26. The Environment Department strongly urges EPA to reconsider this preliminary determination and to promulgate an MCL for perchlorate at a level that will protect human health, including the health of subgroups at greater risk of adverse health effects.

Response: See response to comment code 6120.

Commenter Name: Caroline Baier-Anderson, PhD
Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20941
EPA Comment Code: 6120

Comment: Comments from Environmental Defense Fund on the Preliminary Regulatory Determination on Perchlorate Docket EPA-HQ-OW-2008-0692 Federal Register / Vol. 73, No. 198 / Friday, October 10, 2008

Prepared by Caroline Baier-Anderson, Ph.D. Senior Health Scientist

Submitted to Docket: November 28, 2008

On behalf of Environmental Defense Fund, a non-profit, non-partisan, non- governmental environmental organization that combines law, policy, science and economics to find solutions to today's most pressing environmental problems, we offer the following comments on the Preliminary Regulatory Determination on Perchlorate.

Environmental Defense Fund would like to express our strong disagreement with the Environmental Protection Agency's (EPA) Preliminary Regulatory Determination on Perchlorate, as presented in the Federal Register / Vol. 73, No. 198 / Friday, October 10, 2008. EPA has determined that a national primary drinking water regulation for perchlorate would not present a meaningful opportunity for health risk reduction. We believe that this decision is predicated on a flawed reference dose, and the incorrect application of a physiologically based pharmacokinetic model, leading to the derivation of a faulty health reference level. Below we lay out the details of our criticism, and offer alternative views that justify promulgation of a stronger standard for perchlorate.

Response: Regarding promulgating a perchlorate standard, see response to comment code 6120. Regarding the perchlorate reference dose, see response to comment 28863 under comment code 2110; regarding application of the PBPK model, see responses to comment codes 2400 and 2410; and regarding derivation of the health reference level, EPA derived potential alternative HRLs for 14 life stages (age groups) using the RfD and life stage-specific exposure information in the August 9, 2009, notice (74 FR 41883; USEPA 2009b). These levels range from 1 µg/L to 47 µg/L and are the concentrations of perchlorate in drinking water that may result in total perchlorate exposures (from food and water) greater than the RfD for individuals at each life stage. These HRLs are calculated based on individuals who consume an average amount of perchlorate from food (except for

pregnant women where EPA used a 90th percentile dietary intake estimate), but who consume equal or more water on a per body weight basis than 90 percent of their cohorts.

Commenter Name: Caroline Baier-Anderson, PhD
Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20954
EPA Comment Code: 6120

Comment: EPA Can Reduce Health Risk by Promulgating a Perchlorate Standard

In summary EPA has an opportunity to significantly reduce risks to human health by promulgating a perchlorate standard, providing that the reference dose is based on CDC data, taking into consideration sensitive subpopulations, including women of child-bearing age that are not receiving sufficient iodine, and the fact that hypothyroidism in the US is not only prevalent, but under-diagnosed and under-treated. All else follows from this initial calculation, as a reference dose based on the appropriate consideration of these factors will result in a more realistic estimate of the number of US citizens potentially impacted by perchlorate in drinking water. Such an analysis, based on more realistic assumptions, and newer, more accurate data, will provide concrete support for EPA action.

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Response: Regarding promulgating a perchlorate standard, see response to comment code 6120; regarding the basis for the RfD, see response to comment code 2110; regarding consideration of sensitive subpopulations, see responses to comment codes 5225, 5230, and 5240,

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Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20979
EPA Comment Code: 6120

Comment: November 28, 2008

U.S. Environmental Protection Agency Office of Water Docket (Mailcode: 2822T) 1200 Pennsylvania Avenue, NW Washington, DC 20460

Comments from the NATURAL RESOURCES DEFENSE COUNCIL on the Drinking Water: Preliminary Regulatory Determination on Perchlorate

Docket EPA-HQ-OW-2008-0692 Federal Register / Vol. 73, No. 198 / Friday, October 10, 2008

SUMMARY

On October 10, 2008, EPA announced a preliminary regulatory determination not to set a health-protective standard perchlorate in drinking water.[FN1: 73 Fed. Reg. 0262 (Oct. 10, 2008).] The Federal Register notice states that: "The Agency has determined that a national primary drinking water regulation (NPDWR) for perchlorate would not present 'a meaningful opportunity for health risk reduction for persons served by public water systems.'" EPA sought comments on whether setting a national primary drinking water standard for perchlorate would provide a meaningful opportunity for health risk reduction for persons served by public water systems, on the scientific data and supporting analyses for this determination, and on its use of a revised physiologically-based pharmacokinetics (PBPK) model. With this FR Notice, EPA has proposed a health reference level (HRL) of 15 ppb as the maximum contamination level of perchlorate that could be in drinking water, and still keep daily human consumption levels from exceeding the reference dose (RfD) of 0.7 ug/kg/day.

After careful review of these documents, NRDC concludes that EPA's determination is legally flawed. EPA must regulate a contaminant if it may have an adverse effect on human health, if it is known to occur (or there is a substantial likelihood that the contaminant will occur) in public water systems with a frequency and at levels of public health concern; and if its regulation would present a meaningful opportunity for health risk reduction for persons served by public water systems.[FN2: 42 U.S.C. [section] 300g-1(b)(1)(A).] For perchlorate, each of these three requirements are met, and therefore, underscore that EPA must regulate its presence in drinking water. First, EPA's preliminary regulatory determination acknowledges that perchlorate may adversely affect human health.[FN3: 73 Fed. Reg. 60275 (Oct. 10, 2008).] Second, as explained in more detail below, despite EPA's contention, perchlorate is known to contaminate the drinking water systems serving millions of people at levels where adverse human health effects occur. And third, setting an appropriately stringent MCL will lead to lower levels of perchlorate ingested by hundreds of thousands of infants, thereby offering a concrete and meaningful reduction in human health risks.

Procedurally and scientifically, EPA has made this preliminary determination in an arbitrary and capricious manner. Procedurally, the FR Notice announcing EPA's preliminary determination was issued for public comment even before EPA had received the peer review report on the PBPK model, which EPA used to justify the HRL. Moreover, it is our understanding that EPA is still awaiting peer review comments on the proposed HRL itself. The preliminary determination also fails to address the recommendations of the Science Advisory Board Drinking Water Committee (SAB DWC). Scientifically, the basis for EPA's determination fails to appropriately incorporate data demonstrating population level effects at environmentally relevant levels of exposure. In effect, this data severely undercuts EPA's conclusion that there would not be a sufficient benefit for protecting public health by setting a drinking water standard for perchlorate. The agency's apparent decision to ignore relevant scientific information, in reaching a decision not to regulate this dangerous and widespread drinking water contaminant is not a proper exercise of EPA's decision-making process. Instead of rushing forward without the benefit of full consideration of the most recent scientific evidence (and scientific advice), EPA should carefully review and analyze the results of the peer review of the PBPK model and the HRL, allow the public an opportunity to review and analyze those results, and request an SAB DWC review prior to making a determination on how to address perchlorate contamination. EPA's failure to fully consider the existing data on the effects of perchlorate on vulnerable sub-populations, and short-circuit the process of peer review and public comment on the models upon which their determination is based, is arbitrary and capricious. Furthermore, EPA's conclusion regarding the potential health benefits of setting a drinking water standard for perchlorate is in error, and its preliminary decision not to set a regulatory standard for perchlorate, if finalized, would violate the Safe Drinking Water Act.

Response:
EPA has reversed its October 2008 preliminary determination not to develop an NPDWR for perchlorate and now concludes, based on the analysis presented in the final regulatory determination, that there is a substantial likelihood that perchlorate will occur in public water systems with a frequency and at levels of public health concern. The Agency has determined that regulation of perchlorate presents a meaningful opportunity to reduce health risk for persons served by public water systems.

Please see the response to comment code 6120. EPA disagrees with the commenter's statement that procedurally and scientifically, the preliminary regulatory determination for perchlorate was made in

an arbitrary and capricious manner. EPA considers the best available science when developing drinking water standards, as required by the 1996 amendments to the Safe Drinking Water Act. In applying these principles, "best available" usually refers to the availability at the time an assessment is made. In the August 2009 notice, EPA stated that it was re-evaluating how best to incorporate the PBPK modeling analysis into its evaluation of perchlorate — if at all. The Agency sought comments on ways to use the PBPK modeling analysis to inform the regulatory determination. Regarding the commenter's concern about the peer review of the PBPK model, please see the response to comment code 6400. Additionally, EPA discussed the key scientific issues raised by external peer reviewer commenters on the Interim Drinking Water Health Advisory for perchlorate in the August 2009 notice and in today's notice. A summary of peer review comments and EPA responses on the Interim Drinking Water Health Advisory are available in the docket for today's notice (Docket ID No. EPA–HQ–OW–2009–0297) at http://www.regulations.gov. EPA has further considered peer reviewer and public comments regarding the use of the PBPK model to inform today's regulatory determination for perchlorate, please see response to comment ID 20432 in comment code 5220 for a more detailed discussion.

EPA disagrees that the PBPK model should have been reviewed by the SAB because the model and draft report underwent a formal external peer review by eight experts in accordance with EPA guidance (see response to comment code 6400). Additionally, per SDWA, EPA will consult with the SAB prior to proposal of the perchlorate maximum contaminant level goal and NPDWR.

Please see the response to comment code 5220 for a further discussion of EPA's determination that regulation of perchlorate in drinking water systems presents a meaningful opportunity for health risk reduction for persons served by public water systems.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20982
EPA Comment Code: 6120

Comment: Based upon the evidence in the record, as discussed in greater detail below, NRDC urges EPA to reverse course, and set a national primary drinking water standard for perchlorate that is protective of sensitive sub-populations. EPA should not set a HRL at 15 ppb; rather, given the most current data available, NRDC believes that that a truly health protective standard would fall below 1 ppb.

Response: See response to comment code 6120.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20988
EPA Comment Code: 6120

Comment: NRDC strongly objects to EPA's preliminary determination on perchlorate because the conclusions are not based on a comprehensive review of the best available science (as explained in more detail below) and are not supported by the PBPK model findings, or by EPA's expert scientific

advisors on the Children's Health Protection Advisory Committee.[FN22: Letter from Melanie Marty to Administrator Johnson regarding Preliminary Regulatory Determination on Perchlorate (November 3, 2008, PDF) http://yosemite.epa.gov/ochp/ochpweb.nsf/content/perchlorateletter.htm/$file/PerchlorateLetter.pdf] In fact, drinking water that is contaminated with perchlorate at the HRL would leave infants and young children exposed to excessive and unsafe levels of this toxic chemical.

Response: Please see the response to comment ID 20979 under comment code 6120.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 21003
EPA Comment Code: 6120

Comment: CONCLUSION

EPA should not finalize its preliminary determination not to regulate perchlorate.

Response: See response to comment code 6120.

Commenter Name: Rebecca Connolly
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1882
EPA Comment ID: 21036
EPA Comment Code: 6120

Comment: Dear EPA,

Please stop allowing perchlorate to filter into our drinking water.

Thank you.

Sincerely, Rebecca Connolly 116 Hume Ave. Alexandria, VA 22301

Response: See response to comment code 6120.

Commenter Name: Michael Suttles
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1880
EPA Comment ID: 21037
EPA Comment Code: 6120

Comment: EPA Water Docket

To Whom it May Concern:

I'm a student and a voter in Virginia and I'm concerned about water quality. Perchlorate is a dangerous chemcial often found in water and has been discovered to be present in 37 states. Therefore, it must be regulated in order to protect our health.

Sincerely, Michael Suttles 411A E Howell Ave. Alexandria, VA 22301

Response: See response to comment code 6120.

Commenter Name: Maggie Geist
Commenter Organization: Association to Preserve Cape Cod (APCC)
EPA Document ID: EPA-HQ-OW-2008-0692-2083
EPA Comment ID: 21104
EPA Comment Code: 6120

Comment: November 26, 2008

Water Docket Environmental Protection Agency Mail Code: 2822T 1200 Pennsylvania Ave., NW Washington, DC 20460 RE: Docket ID No. EPA-HQ-OW-2008-0692

To Whom It May Concern:

The Association to Preserve Cape Cod (APCC) is a non-profit environmental organization dedicated to the preservation of Cape Cod's natural resources and quality of life. Founded in 1965 and currently representing over 5,500 members, APCC is the oldest and largest environmental organization on Cape Cod.

On behalf of APCC, I am pleased to submit comments on the Preliminary Regulatory Determination on Perchlorate in Drinking Water proposed by USEPA. APCC urges USEPA to reconsider its determination to not regulate perchlorate. There are a significant number of water resources across-the country that contain perchlorate; 35 states have detected dangerous levels of perchlorate in drinking water. The full extent of the pervasiveness of perchlorate is still unknown. In addition to drinking water, it is also found in produce and dairy products, likely coming from water used to irrigate crops and water livestock. Perchlorate is also extremely persistent, meaning it has the potential to migrate far from the source of contamination, polluting entire watersheds.

The health consequences of ingesting perchlorate are significant, largely impact infants, and can be transferred maternally to a fetus. Perchlorate causes a reduction of the thyroid hormone production. The thyroid hormone is critical for muscle and brain development. Where protecting the health and development of children is of paramount importance, such risks from perchlorate are unacceptable. Establishing a regulatory limit on perchlorate in drinking water is an important step in reducing this risk nationwide.

Sincerely,

Maggie Geist

Response: See response to comment code 6120.

Commenter Name: Peggy Shiffrin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2084
EPA Comment ID: 21105
EPA Comment Code: 6120

Comment: Peggy Kobacker Shiffrin 2811 Chesterfield Place, NW Washington, DC 20008

November 20, 2008

Water Docket, EPA, Mailcode 2822T 1200 Pennsylvania Avenue, NW Washington, DC 20460

Docket ID No. EPA-HQ-OW-2008-0692

To whom it may concern:

I urge you to reverse your decision and set a federal limit n perchlorate in drinking water. Perchlorate is a nationwide problem and has health impacts at lower levels than previously thought. Please protect public health, especially infants and children, by regulating perchlorate.

Thank you,

Peggy Shiffrin

Response: See response to comment code 6120.

Commenter Name: Teresa Jordan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2086
EPA Comment ID: 21107
EPA Comment Code: 6120

Comment: 3152 Shad Court Simi Valley, CA 93063 November 16, 2008

Water Docket USEPA Mailcode: 2822T 1200 Pennsylvania Avenue, N.W. Washington, DC 20460

Re: DOCKET ID No. EPA-HQ-OW-208-0692 (Preliminary Regulatory Determination on Perchlorate -- Reopening of Public Comment Period (Novemeber 28, 2008 Deadline)).

Dear Mr. Grumbles, and Mr. Burneson:

I am writing to ask that the Agency initiate development of a national regulation for perchlorate in drinking water.

Mr. Grumbles and Mr. Burneson, as a concerned citizen who has followed the significant impacts to people's and animals' health from water, soil, and air contamination due to DOW, NASA, and Rockwell International/Boeing Company rocket engines and nuclear reactors testing, lasers and other activities on the Santa Susana Field Laboratory (the SSFL, located in Simi Hills, in Ventura

County, California) for 19+ years, I was shocked when I read that the Agency would not be regulating perchlorate in drinking water systems around the Nation beacuse the determination significant ramifications for the County of Ventura, and, most especially, the City of Simi Valley!!!

Mr. Grumbles and Mr. Burneson, if I ever thought there was hope to finally have the SSFL included in the USEPA's Superfund List because of the Agency's cumulative findings, such grave news -- this determination coming years after perchlorate was included on the first (March 2, 1998) and second (February 24, 2005) Contaminant Candidate Lists (CCLs) -- just snuffed out the small light at the end of this very long tunnel! What travesty for the public trust, and the environmental justice program!!!

Mr. Grumbles and Mr. Burneson, this determination will allow the Ventura Countrywide MS4 NPDES Permit, and the municipal NPDES permits for the Cities of Thousand Oaks and Simi Valley, and the Camarillo Sanitary District waste water treatment plants to breeze through the Los Angeles Regional Water Control Board (LARWQCB) public review and comment period, and public hearing next time around -- no wonder the two subjects dropped off the radar.

Response: See response to comment code 6120.

Commenter Name: Frederick Behnke Jr.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2087
EPA Comment ID: 21110
EPA Comment Code: 6120

Comment: November 24, 2008

Water Docket, EPA Mail Code 2822T 1200 Pennsylvania Ave Washington DC 20460 Attention: Docket No. EPA-HQ-OW-2008-0692

To Whom It May Concern:

Please keep our drinking water safe by regulating the amount of perchlorate allowed in our drinking water. There has been scientific proof that perchlorate can lead to thyroid problems in pregnant women, newborns, and infants. A primary drinking water regulation is needed to protect the public health. Sincerely,

Frederick E Behnke, Jr. 1470 Mordor Lane Hanover MD 21076

Response: See response to comment code 6120.

Commenter Name: Anne Eberhardt
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2088
EPA Comment ID: 21111
EPA Comment Code: 6120

Comment: Water Docket, EPA Mail Code 2822T 1200 Pennsylvania Ave Washington, DC 20460 Attn: DOcket ID EPA-HQ-OW-2008-0692

To Whom it May Concern

It has come to my attention that the EPA has announced its intention to not regulate perchlorate in drinking water.

Please reverse that decision immediately. Do not ruin our drinking water which has always been good. Please regulate it.

Anne Eberhardt 1213 Tacoma St Allentown, PA 18109

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2089
EPA Comment ID: 21112
EPA Comment Code: 6120

Comment: Perchlorate contamination is a nationwide problem which needs to be addressed. Perchlorate has health impacts at lower levels than previously thought. A National Primary drinking water regulation is needed to protect our drinking water from pollutants.

The Food and Drug Administration found perchlorate in 74% of foods it tested. We don't need more perchlorate coming from our drinking water.

For the health of everyone something need to be done, so please keep perchlorate out of our drinking water.

Sincerely

Response: See response to comment code 6120.

Commenter Name: Tina, Mona, and Ahmed Saleh
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2090
EPA Comment ID: 21113
EPA Comment Code: 6120

Comment: Water Docket, EPA Mail Code 2822T 1200 Pennsylvania Ave. Washington, DC 20460 Attn: Docket ID No. EPA-HQ-OW-2008-0692

To Whom it May Concern,

We need good, clean, purified water to keep this nation healthy. My mother has been going to the Doctor's for a whole year now because the area of her kidney has been bothering her and the

Doctor's say it's due to the unhealthy, unpurified water she has been drinking. Perchlorate contamination is a worldwide problem and has health impacts at lower levels than previously thought. Its already effecting 37 states. 37 states! That's more than half of the U.S. We need to stay healthy, we need cleaner water.

Sincerely, Tina Saleh Mona Saleh Ahmed Saleh 1635 E. Greanleaf St. Allentown, PA 18109

Response: See response to comment code 6120.

Commenter Name: Ellen Blaschinski, M.B.A., R.S.
Commenter Organization: Regulatory Services Branch, Connecticut Department of Public Health
EPA Document ID: EPA-HQ-OW-2008-0692-2091
EPA Comment ID: 21117
EPA Comment Code: 6120

Comment: EPA's opportunity to address perchlorate is substantial from a public health perspective given the risks this chemical can pose to early life development and its potential for occurrence in public water supplies. Sensitive test methods exist as do practical treatment options. Therefore, we urge EPA to reconsider its decision to not regulate perchlorate. In that reevaluation, EPA should utilize methodologies that ensure protection of all potentially sensitive receptors from the anti-thyroid effects of this chemical.

Please let us know if you would like additional information regarding the Connecticut Department of Public Health's comments on this important matter.

Sincerely, Ellen Blaschiriski, M.B.A., R.S., Chief, Regulatory Services Branch

Response: See response to comment code 6120.

Commenter Name: Bonnie Ludwick
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2092
EPA Comment ID: 21118
EPA Comment Code: 6120

Comment: OW-2008-0692=

To Whom It May Concern

Please regulate Perchlorate out of our drinking water now! Thanks Bonnie S. Ludwick 30 W. High St Hellertown, PA 18055

Water Docket, EPA, Mailcode 2822T 1200 Pennsylvania Ave. Washington, DC 20460 Attn: Docket ID No. EPA-HQ-OW-2008-0692

Response: See response to comment code 6120.

Commenter Name: (illegible)

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2093
EPA Comment ID: 21119
EPA Comment Code: 6120

Comment: -OW-2008-0692 11/13 Dear EPA,

Learning of the side effects of perchlorate contaminations (thyroid issues, birth deffects, loss of [illegible] etc) that come from military bases, fireworks, construction sites, and so on. If you could do a regular water check (weekly or daily)....Just to make sure the water that your fellow citizens consume daily even babies OR at least inform us ASAP that the levels are high so we could at least use bottled water (while you filter the water) it would prevent so many problems.

Thank you, high school student nurses aid

Response: See response to comment code 6120.

Commenter Name: Juanita Velez
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2094
EPA Comment ID: 21120
EPA Comment Code: 6120

Comment: 631 Oakcrest Wyoming MI 49508

Stephan Johnson,

Clean Water is important to every living thing and its important to keep the water safe + pure for the future generations. To help regulate green house gas emissions under the Clean air act.

thank you Juanita Velez

Response: This is not a comment, no response is needed.

Commenter Name: Clair Edwards
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2095
EPA Comment ID: 21121
EPA Comment Code: 6120

Comment: Dear EPA,

Please keep toxins out of our water these are harmful to our kids!!!

Thank you Clair Edwards 2422 Taylor Ave Alex. VA 22302

Response: See response to comment code 6120.

Commenter Name: John Hall
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2096
EPA Comment ID: 21122
EPA Comment Code: 6120

Comment: To: EPA

Perchlorate is unsafe -- hurts kids, toxic.

Please stop.

John Hall 213 Woodland Ter Alexandria VA 22303

Response: See response to comment code 6120.

Commenter Name: Andrew Freed
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2097
EPA Comment ID: 21123
EPA Comment Code: 6120

Comment: U.S. Environmental Protection Agency,

My name is Andrew Freed and I am writing you in regards to an issue that has been brought to my attention recently. A young lady I encountered informed me of the epidemic surrounding perchlorate in drinking water. She educated me on the concerns and factors if we do not regulate the amounts of perchlorate in our drinking water.

One of the concerns she brought up is that perchlorate contamination is a nationwide problem. Not only does this effect my drinking water personally but this concerns me because, coming from a larger family, we are spread nationwide and their health is just as important to me as my own.

Another concern is that the EPA is ignoring the fact that lower levels of perchlorate in our drinking water does have impacts on health, more than they previously thought. One of the risks is impairment to the thyroid gland. Many people aren't aware of the importance of that gland. It not only controls growth it also controls development and metabolism. When tampered with, these impacts are especially harmful to children and fetuses.

And a factor that really stuck home is the lack of concern for our nation from the EPA. In our world today, we have to start somewhere in, order to make change. Our newly appointed president wants to make change and this might be a step in the right direction. A national primary drinking water regulation is needed to protect public health. Citizens of the United States are not aware of many of the risks they face everyday. We rely on government agencies to ensure our safety when it comes to everyday exposure to things we take for granted like the water:we drink and the air we breathe.

All I am asking for is that you take a look at the concerns and think to yourself would you or your loved ones want to drink water that is contaminated?

Thank you for your time. Sincerely, Andrew Freed

Response: See response to comment code 6120.

Commenter Name: Edward and Colleen Flok
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2098
EPA Comment ID: 21124
EPA Comment Code: 6120

Comment: Water Docket, EPA Mail Code 2822T 1200 Pennsylvania Ave Washington, DC 20460 Attn: Water Docket ID No. EPA-HQ-OW-2008-0692

To Whom It May Concern

Perchlorate is a widespread contaminate. It is a nationwide problem, that has health impacts at lower levels than previously thought. Perchlorate contamination threatens public health. Traces of Perchlorate have been detected in people, the foods we eat, and groundwater.

I am now aware the United States Environmental Protection Agency (EPA) has announced its intention not to regulate Perchlorate in drinking water. I am writing this letter to ask that the EPA reverse there decision. A national primary drinking water regulation is needed to protect public health.

Thank you. Respectfully, Dr. Edward Flok 1335 Jefferson Street Hellertown, Pa. 18055 610-838-4851 Email: eddieflok57@gmail.com

Respectfully, Colleen M. Flok 1335 Jefferson Street Hellertown, Pa. 18055 Email: colleenf58@aol.com

Response: See response to comment code 6120.

Commenter Name: Ann Mowrey
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2099
EPA Comment ID: 21125
EPA Comment Code: 6120

Comment: November 20, 2008 To Whom It May Concern:

I am concerned with keeping Perchlorate out of our drinking water. Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought. A national primary drinking water regulation is needed to protect public heath.

Thank you Ann Mowrey 136 Roth Ave. Hellertown, PA 18055

Water Docket, EPA Mail Code 2822T 1200 Pennsylvania Ave Washington, DC 20460 Attn: Water Docket ID No. EPA-HQ-OW-2008-0692

Response: See response to comment code 6120.

Commenter Name: Kristin Verrastro
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2100
EPA Comment ID: 21126
EPA Comment Code: 6120

Comment: U.S. Environmental Protection Agency,

My name is Kristin Verrastro and I am writing you in regards to the recent concerns of regulating perchlorate in our nations drinking water. I am a resident of Pennsylvania and have been recently informed about this growing problem.

I am not sure if you are aware of the dangers of the perchlorate being in our drinking water but it does not just affect a specific area. It is a nationwide problem and impacts health issues at lower levels than previously thought. One of the health problems that perchlorate can impair is the thyroid gland. As a person who deals with thyroid issues personally this has raised a red flag in my life. If you are not aware, the thyroid glad controls growth, development and metabolism, which can be extremely harmful if tampered with to children and fetuses.

Also speaking as a human being needing water to survive everyday life, the excessive amounts of perchlorate in our drinking water needs to be regulated to protect public health. I am 26 years old woman and some day would like to have children and the risk that they may become sick because of something that we as a nation could have fixed is also something that raises a red flag in my life.

All I am asking for is that you take a look at the concerns and think to your self, would you or your loved ones want to drink water that is contaminated?

Thank you for your time.

Kristin E. Verrastro

Water Docket, EPA Mail Code 2822T 1200 Pennsylvania Ave Washington, DC 20460 Attn: Water Docket ID No. EPA-HQ-OW-2008-0692

Response: See response to comment code 6120.

Commenter Name: Kemmerer Family
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2101
EPA Comment ID: 21127
EPA Comment Code: 6120

Comment: Water Docket, EPA Mail Code 2822T 1200 Pennsylvania Ave Washington, DC 20460 Attn: Water Docket ID No. EPA-HQ-OW-2008-0692

To the US Environmental Protection Agency,

You need to reverse your decision and regulate perchlorate in drinking water. Perchlorate contamination is a nationwide problem and has health effects at lower levels than previously thought. A national primary drinking water regulation is needed to protect public health. Please reconsider your decision. This is a big health issue.

The Kemmerer Family

Response: See response to comment code 6120.

Commenter Name: Katie and Frank Nemeth Hummer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2102
EPA Comment ID: 21128
EPA Comment Code: 6120

Comment: November 13, 2008

Water Docket, EPA Mail Code 2822T 1200 Pennsylvania Ave Washington, DC 20460 Attn: Water Docket ID No. EPA-HQ-OW-2008-0692

Attention: U.S. Environmental Protection Agency (EPA):

I am writing to inform you of some recent information I have obtained from an outside source. Did you know that perchlorate is a nationwide problem and has health impacts at lower levels than previously thought? Did you know that a national primary drinking water regulation is needed to protect public health?

It is your duty to take close investigation on this matter that we, as the people, have support and protection in this issue. Please take this information and investigate solutions on this serious issue concerning something we all need for survival.

Cordially, Katie Hummer Frank Nemeth

Response: See response to comment code 6120.

Commenter Name: Sandra Hoag
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2103
EPA Comment ID: 21129
EPA Comment Code: 6120

Comment: 11/18/08

Sandra L. Hoag 806 Crescent Drive Alexandria, VA 22302

Water Docket, EPA, Mailcode 2822T 1200 Pennsylvania Ave. NW Washington, DC 20460 Docket ID No. EPA-HQ-0W 2008-0692

To Whom it May Concern:

I urge you to reverse your decision and set a federal limit for perchlorate in drinking water. Perchlorate is a nationwide problem and has greater health impacts at lower levels than previously thought. Please protect public health, especially infants and children, by regulating perchlorate.

Sincerely, Sandra Hoag

Response: See response to comment code 6120.

Commenter Name: April Verlo
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2104
EPA Comment ID: 21130
EPA Comment Code: 6120

Comment: 11/18/08

To: EPA Water Docket

I am an environmental scientist and concerned about perchlorate. It affects children and is widespread. Please see that it is regulated.

April Verlo 401 Tennessee Alexandria, VA 22305

Response: See response to comment code 6120.

Commenter Name: Elizabeth Johnson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2105
EPA Comment ID: 21131
EPA Comment Code: 6120

Comment: Elizabeth Johnson 2704 Davis Avenue Alexandria, VA 22302 November 19, 2008

Water Docket, EPA, Mailcode 2822T 1200 Pennsylvania Avenue, NW Washington, DC 20460 Re: Docket ID No. EPA-HQ-OW-2008-0692

To Whom It May Concern:

I urge you to reverse your decision and set a federal limit for perchlorate in drinking water. Perchlorate is a nationwide problem and has health impacts at lower levels than previously thought.

Please protect public health, especially the health of infants and children, by regulating perchlorate. With five grandchildren I am particularly concerned about the impact of your decision on the standards set for the water they drink.

Sincerely, Elizabeth Johnson

Response: See response to comment code 6120.

Commenter Name: Toni Soule
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2106
EPA Comment ID: 21132
EPA Comment Code: 6120

Comment: Dear EPA,

Please regulate toxins in our drinking water, especially perchlorate, which is dreadful!

Sincerely, Toni Soule 2400 Clemson Mills Rd Alex., VA 22302

Response: See response to comment code 6120.

Commenter Name: Lorraine Keir
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2107
EPA Comment ID: 21133
EPA Comment Code: 6120

Comment: 3307 Elmore Drive Alexandria, VA 22302

November 16, 2008

Water Docket, EPA, Mailcode 2822T 1200 Pennsylvania Avenue, NW Washington, DC 20460
Docket ID No. EPA-HQ-OW-2008-0692

To Whom It May Concern:

I urge you to reverse your decision and set a federal limit for perchlorate in drinking water. I have a small child and am concerned about the effects of perchlorate on her health and development. Please protect public health, especially those of infants and children like my daughter, by regulating perchlorate.

We have a right to clean drinking water and the government should do all in it's power to ensure our water is safe. Thank you for your consideration.

Sincerely,

Lorraine P. Keir

Response: See response to comment code 6120.

Commenter Name: J.B. Poersch
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2108
EPA Comment ID: 21134
EPA Comment Code: 6120

Comment: Dear EPA,

Regulate perchlorate. Its too big a risk for my family.

Sincerely J.B. Poersch 608 Woodland Tr. Alexandria, VA 22302

Response: See response to comment code 6120.

Commenter Name: Laura Ahehan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2109
EPA Comment ID: 21135
EPA Comment Code: 6120

Comment: Dear EPA,

Please regulate perchlorate and other harmful toxins. Our neighborhood knows it is dangerous for our children.

Laura Ahehan 2414 Davis Ave. Alexandria, VA 22302

Response: See response to comment code 6120.

Commenter Name: Michael Aldanli
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2110
EPA Comment ID: 21136
EPA Comment Code: 6120

Comment: Dear EPA,

As a concerned citizen, I believe perchlorate should be eliminated from the environment to the maximum extent feasible.

Michael Aldanli 3400 Alabama Ave. Alexandria, VA 22305

Response: See response to comment code 6120.

Commenter Name: George B.

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2113
EPA Comment ID: 21954
EPA Comment Code: 6120

Comment: Nov. 20, 2008

E.P.A.

Please work to regulate or better yet eliminate perchlorate from everyone's drinking water.

Thanks,

George B. [illegible] 1044 Springhill Way Gambrills, MD 21054 301-621-7881

Response: See response to comment code 6120.

Commenter Name: Ron W
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2114
EPA Comment ID: 21956
EPA Comment Code: 6120

Comment: Nov. 17, 2008

Dear EPA

I urge you to regulate the amount of perchlorate in our drinking water supply.

Sincerely,

Ron W [illegible] 3324 [illegible] Lane Brookeville, Md 20833

Response: See response to comment code 6120.

Commenter Name: T Siegel
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2115
EPA Comment ID: 21958
EPA Comment Code: 6120

Comment: EPA Water Docket:

I am a Wash DC voter. Perchlorate is a dangerous chemcial found in 37 states - it gets into water and therefore must be regulated.

T. Siegel 1383 28th St NW Wash DC 20007

Response: See response to comment code 6120.

Commenter Name: Matt Lewis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2116
EPA Comment ID: 21965
EPA Comment Code: 6120

Comment: To All Readers,

Perchlorate is a harmful chemical found in our drinking water. It is used in Rocket fuel and explosives. Every day, citizens ingest thousands of gallons nationally. If something is not done soon, This great country will be left a barren wasteland with no humans to care for it and all our efforts will have been wasted. Perchlorate can cause massive problems both physically and mentally to any human that ingests it.

Response: See response to comment code 6120.

Commenter Name: Matt Lewis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2116
EPA Comment ID: 21967
EPA Comment Code: 6120

Comment: This country strives not on its technological booms, but the minds that drive them. If we do not act now, it'll soon be too late and what use will these technological advances be to us then. Without the bright minds of our citizens, what use is a government who wouldn't act when it had the chance.

If the EPA does not do something to prevent further problems now, then there is no point in allowing them to stay as a federal agency anymore. The EPA has a responsibility to act now and as such should proceed with all haste. No Bureaucratic procedure or code should stop them. No effort should be made to stop them from proceeding to fulfill their duty to this great country.

There are many sources of perchlorate contamination including many military bases, fireworks manufacturers, and blasting at construction sites. If there were more routine testing then perhaps the problem could be more properly identified. Currently perchlorate has been found in 37 states, and in public water systems serving over 20 million people.

Respectfully, Matt Lewis

Response: See response to comment code 6120.

Commenter Name: Christine Wojciechowski
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2118
EPA Comment ID: 21987
EPA Comment Code: 6120

Comment: November 14, 2008

To Whom It May Concern:

Perchlorate is a harmful chemical that can cause health problems if ingested. This chemical should not be in our drinking water. We need regulation to protect public health.

Thank you, Christine Wojciechowski

Response: See response to comment code 6120.

Commenter Name: John Sherry
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2120
EPA Comment ID: 21990
EPA Comment Code: 6120

Comment: Water Docket, EPA Mailcode 2822T, 1200 Pennsylvania Ave., Washington, D.C. 20460

We live very close to a military base and to dump site. We need routine testing and a drinking water regulation

Thank you John Sherry

Response: See response to comment code 6120.

Commenter Name: Eugene A. Smell
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2122
EPA Comment ID: 21998
EPA Comment Code: 6120

Comment: 20 November 2008

To: EPA

Please continue to regulate perchlorate in drinking water.

Thank you

Eugene A. Smell

Response: See response to comment code 6120.

Commenter Name: Barbara A. Smell
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2123

EPA Comment ID: 21999
EPA Comment Code: 6120

Comment: November 20, 2008

EPA

To whom it may concern:

Please continue to regulate perchlorate in drinking water.

Barbara A. Smell

Response: See response to comment code 6120.

Commenter Name: Sarah Favrao
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2124
EPA Comment ID: 22011
EPA Comment Code: 6120

Comment: November 11. 2008

To whom it may concern:

I am writing to urge the EPA to reverse their decision to not regulate perchlorate in our drinking water. Studies have shown that this it is a nationwide problem with ground water contamination, and has detrimental health effects for all, but especially fetuses and young children. From what I have read from Clean Water Action's literature, I believe perchlorate should be regulated, to protect my health and my family's health.

Sarah Favrao

Response: See response to comment code 6120.

Commenter Name: Robert J
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2125
EPA Comment ID: 22012
EPA Comment Code: 6120

Comment: 11-10-08

To: Water Docket EPA, mailcode 2822T 1200 Penn. Ave Wash DC, 20460 ATTN: Docket ID No EPA-HQ-OW-2008-0692

Dear Sirs,

I believe perchlorate contamination is a national problem and has health impacts at lower levels than previously thought.

A national primary drinking water regulation is needed to protect the public health.

Regards Robert J [illegible] 103[illegible] Askewton Road Severna Park, MD. 21146

Response: See response to comment code 6120.

Commenter Name: Elaine
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2127
EPA Comment ID: 22013
EPA Comment Code: 6120

Comment: November 17, 2008

EPA,

I am a concerned Alexandria Virginia resident.

I learned about your decision not to regulate perchlorate and am upset with this decision

It is a threat to human health and I asking you to reconsider and regulate.

Thank you Elaine [illegible]

Response: See response to comment code 6120.

Commenter Name:
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2128
EPA Comment ID: 22014
EPA Comment Code: 6120

Comment: To whom it may concern:

Perchlorate is not something I want in my water. For the sake of our nation's young people, please consider regulating this threat to our DC water supply!

Sincerely, [illegible] 3609 N Street Washington, DC 20007

Response: See response to comment code 6120.

Commenter Name: Anna Sannes
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2129
EPA Comment ID: 22015

EPA Comment Code: 6120

Comment: Dear EPA,

I'd just like to take this opportunity to remind you how important it is that we keep perchlorate out of our water systems. As a daycare worker, I spend most of my time with children, and the thought of them being hurt developmentally, by water, is frightening. Please help keep our children safe; keep perchlorate out of the water.

Thanks, Anna Sannes LXR 217 Georgetown University Box 578853 Washington, DC 20057

Response: See response to comment code 6120.

Commenter Name: Katherine Rogers
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2130
EPA Comment ID: 22016
EPA Comment Code: 6120

Comment: To EPA -

Please don't put perchlorate in our water.

3263 O St, NW Washington, DC 20007

Katherine Rogers

Response: EPA does not put perchlorate into water. EPA has determined that perchlorate in drinking water requires regulation. See response to comment code 6120.

Commenter Name: Courtney Stonestreet
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2131
EPA Comment ID: 22017
EPA Comment Code: 6120

Comment: 12 November 2008

Courtney Stonestreet 3378 Martha Custis Drive Alexandria, Virginia 22302

Dear EPA -

We need clean, healthy water in Virginia! Perchlorate needs to be labeled as a harmful toxin and kept out of our drinking. Please do you part with the public's health in mind and keep this chemical out of the water.

Sincerely, Courtney Stonestreet

Response: See response to comment code 6120.

Commenter Name:
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2132
EPA Comment ID: 22018
EPA Comment Code: 6120

Comment: To: EPA Water Docket

I am a Virginia voter and a grandmother concerned about the state of the planet our grandchildren will inherit.

Perchlorate is a dangerous chemical found in 37 states. Therefore, since affects children when it gets into water, it should be regulated.

Sincerely,

[illegible] 1510 Dogawood Drive Alexandria, VA 22302

Response: See response to comment code 6120.

Commenter Name: Lani Weatherhead
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2133
EPA Comment ID: 22019
EPA Comment Code: 6120

Comment: 11/12/08

Dear EPA,

Please don't put perchlorate in my water. It will hurt my baby. Please regulate what you are allowing to get into the water.

Thank you,

Lani Weatherhead 3755 Gunston Alexandria, VA 22302

Response: EPA is not putting perchlorate into your water. EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Jackie Draghi
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2134
EPA Comment ID: 22020
EPA Comment Code: 6120

Comment: 1/22/08

Dear EPA,

Please regulate perchlorate and do routine testing for it.

Sincerely, Jackie Draghi 3775 Gunston Road Alexandria, VA 22302

Response: See response to comment code 6120.

Commenter Name: William Webner
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2135
EPA Comment ID: 22021
EPA Comment Code: 6120

Comment: November 2008

To: EPA Water Docket -

I am a voter and DC resident. Perchlorate is a dangerous chemical found in 37 states. It msut be regulated because it gets into water.

William Webner 1237 30th Street Wash, DC 2007

Response: See response to comment code 6120.

Commenter Name: Gladys Billups
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2136
EPA Comment ID: 22022
EPA Comment Code: 6120

Comment: TO: EPA From: Gladys Billups

To Whom It May Concern,

As a citizen concerned about passing a stringent and decisive clean water act by congress, I request that you work with the organization Clean Water Action to ban the use of per chlorate. We as a nation should have access to clean and safe water without toxic chemicals.

Respectfully, Gladys Billups

Response: See response to comment code 6120. Banning the use of perchlorate is outside the scope of this regulatory determination.

Commenter Name: Kimberly Feeney
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-2140
EPA Comment ID: 22023
EPA Comment Code: 6120

Comment: November 10, 2008

Environmental Protection Agency 1200 Pennsylvania Avenue Washington, D.C. 20460

Re: Perchlorate Contamination of Drinking Water

To Whom It May Concern:

Perchlorate contamination of drinking water is a public health issue. Until each state, in the United States, addresses perchlorate contamination, I believe the EPA must regulate national primary drinking water.

Perchlorate contamination of drinking water is unacceptable.

Sincerely, Kimberly Feeney

Response: See response to comment code 6120.

Commenter Name: Deborah Honecker
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2141
EPA Comment ID: 22024
EPA Comment Code: 6120

Comment: Nov. 6, 2008

To Whom It May Concern,

Please consider the risks involved with perchlorate contamination. Citizens expect the EPA to monitor water quality and locate sources of water contamination. The military, industry, and other interests have proven themselves unwilling or inept at self-monitoring, which makes your work that much more important. The health and safety of millions of citizens are dependent on actions taken by the EPA.

Thank you, Deborah Honecker 521 Evergreen Rd. Severna Park, MD 21146

Response: See response to comment code 6120.

Commenter Name: Linda L Ferguson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2142
EPA Comment ID: 22025
EPA Comment Code: 6120

Comment: Dear EPA,

I urge you to regulate the amount of perchlorate in our drinking water supply.

Sincerely, Linda L. Ferguson 602 Persimmon Ct Severna Park, MD 21146

Response: See response to comment code 6120.

Commenter Name: Ellie Milleker
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2143
EPA Comment ID: 22026
EPA Comment Code: 6120

Comment: Ellie Milleker 112 A Askewton Rd Severna Park, MD

Water Docket EPA Mailcode 2822T 1200 Pennsylvania Ave. Washington, D.C. 20460

Re: Docket ID No. EPA-HQ-OW-2008-0692

I am writing to voice my strong opposition to not put regulations on perchlorate in drinking water. Perchlorate contamination is a nationwide problem. A national primary drinking water regulation is needed to protect public health.

Sincerely, Ellie Milleker

Response: See response to comment code 6120.

Commenter Name: Kimberly & Justin Vance Carter
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2144
EPA Comment ID: 22027
EPA Comment Code: 6120

Comment: November 20, 2008

Water Docket EPA Mailcode 2822T 1200 Pennsylvania Ave. Washington, DC 20460 ATTN: Docket ID No. EPA-HQ-0W-2008-0692

Dear Sir/Madam:

I understand that the EPA does not intend to regulate perchiorate in drinking water. I understand that perchlorate is a human health hazard causing damage to the thyroid gland. I also understand that perchlorate is currently detected in 37 states and in public drinking water thus affecting over 20 million Americans. This is unacceptable.

I urge the EPA to rethink it's position on this issue. The U.S. is the wealthiest nation on the planet and there is no excuse for Americans to be exposed to this toxin by simply drinking a glass of water. Thank you in advance for your prompt attention to this matter.

Sincerely, Kimberly Carter & Justin Vance

Response: See response to comment code 6120.

Commenter Name: Breona Keller
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2145
EPA Comment ID: 22028
EPA Comment Code: 6120

Comment: Dear EPA,

I think you should try to cleanse the water that we wash and drink in. If we want our world back to normal we have to sacrifice a lot of things. As I was reading the sheet, it said perchlorate is a harmful chemical used in rocket fuel and explosives. And it impacts are especially harmful to children and fetuses. Stop doing harm to our planet and to the human beings that live in it. Just take it out of our water.

Thank You, Breona Keller

Response: See response to comment code 6120.

Commenter Name: Linda E. Lozier
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2146
EPA Comment ID: 22029
EPA Comment Code: 6120

Comment: November 6, 2008 U.S. Environmental Protection Agency

Sir / Ma'am,

It is my understanding that the EPA intends not to regulate the levels of Per chlorate in our drinking water. I urge you to reconsider this position. A standard must be set. Per chlorate is a harmful chemical that is used in rocket fuel and explosives. It should not be present in our children, or ourselves. Per chlorate affects the thyroid gland and may severely impair growth and development of fetuses and children. With this said, regulation is a must. This should not be allowed to go unmonitored. Please reconsider your position, for yourself, and our future. Thank you for your time and consideration.

Respectfully yours, Linda E. Lozier

Response: See response to comment code 6120.

Commenter Name: E. Breem
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2147
EPA Comment ID: 22030
EPA Comment Code: 6120

Comment: November 10, 2008

To U.S. EPA,

Please keep perchlorate out of drinking water!

Help protect our children from the harmful chemical!

Thank you, E. Breem 103 Askewton Rd. Severna Park, MD 21146

Response: See response to comment code 6120.

Commenter Name: John Vernon
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2148
EPA Comment ID: 22031
EPA Comment Code: 6120

Comment: 11/9/08

To the EPA -

I strongly urge reconsideration of the decision not to regulate perchlorate in drinking water. This is an important public health issue, regardless of the simple minded tree huggers. Feel free to have the new Administrator give me a call or drop me a line, any time. Keep up your good work!

Sincerely, John Vernon 107 Askewton Rd. Severna Park, MD 21146

Response: See response to comment code 6120.

Commenter Name: Katie Milleker
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2149
EPA Comment ID: 22032
EPA Comment Code: 6120

Comment: Katie Milleker 112A Askewton Rd. Severna Park, MD 21146

Water Docket EPA Mailcode 2822T 1200 Pennsylvania Ave. Washington, D.C> 20460

Re: Docket ID No. EPA-HQ-OW-2008-0692

I am writing to implore you to overturn your decision regarding not regulating perchlorate in drinking water! I am a lifelong resident of Maryland and I am a holistic healthcare practitioner. Health and nutrition is a priority in my family and while I can control what we eat, I have always assumed we have safe and clean drinking water. Since I believe that perchlorate is a harmful chemical, it is the responsibility of the EPA to regulate specific levels of this chemical in our drinking water. By being proactive in this regard we shall avoid future health problems and save not only countless dollars for health care but more importantly, citizens health and well-being.

Sincerely, Katie Milleker

Response: See response to comment code 6120.

Commenter Name: Nancy
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2150
EPA Comment ID: 22034
EPA Comment Code: 6120

Comment: 11/11/08

To the powers that be,

I write as a concerned citizen regarding perchlorate contamination. I understand that it may be present in our water supply, especially near military installations. I live in Anne Arundel Country, Md. - home to Ft. Meade, as well as mercury contamination sites. And for 35 years, I have worked in the field of early childhood disabilities.

Whatever control we may have over harmful substances in our environment is worth achieving. Please consider the safety cautions related to perchlorate contamination.

Thank you Nancy [illegible]

Response: See response to comment code 6120.

Commenter Name: Taylor M.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2151
EPA Comment ID: 22041
EPA Comment Code: 6120

Comment: Dear EPA,

I believe that it is important to keep our water safe and healthy. Having perchlorate is not healthy at all. I'd rather not have my body damaged just because I drank some water. Please fix this problem!

Thank you Taylor. M. [no surname]

Response: See response to comment code 6120.

Commenter Name: Lewis W. Billups
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2152
EPA Comment ID: 22044
EPA Comment Code: 6120

Comment: TO: EPA From: Lewis W. Billups

To Whom It May Concern,

As a citizen concerned about passing a stringent and decisive clean water act by congress, I request that you work with the organization Clean Water Action to ban the use of per chlorate. We as a nation should have access to clean and safe water without toxic chemicals.

Respectfully, Lewis W. Billups

Response: See response to comment code 6120.

Commenter Name: George Cooper
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2153
EPA Comment ID: 22045
EPA Comment Code: 6120

Comment: Dear EPA,

I support imposing a standard on the regulation of perchlorate in drinking water.

Sincerely, George Cooper 3612 Oval Dr Alexandria, VA 22305

Response: See response to comment code 6120.

Commenter Name: Laura Ricard
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2154
EPA Comment ID: 22057
EPA Comment Code: 6120

Comment: To Whom It May Concern

As a concerned citizen who cares deeply about environmental issues I urge you to list perchlorate as a chemical sufficiently toxic to limit its presence in drinking water. Given our recent change in leadership I am hopeful that you will feel emboldened to take a stronger stance to protect our environment.

Regards, Laura Richard, PA C 516 Tennessee Ave Alexandria, VA 22305

Response: See response to comment code 6120.

Commenter Name: Sheila C Joy
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2155
EPA Comment ID: 22070
EPA Comment Code: 6120

Comment: 11/17/08

To: EPA Water Docket

I am a Virginia voter, perchlorate is a dangerous chemical which should be regulated. It occurs in 37 states and adversely affects children.

Sincerely, Sheila C Joy 3418 Old Dominion Blvd Alex VA 22305

Response: See response to comment code 6120.

Commenter Name: Kelsey Ogburn
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2156
EPA Comment ID: 22072
EPA Comment Code: 6120

Comment: 11/13/08

EPA

You must continue to regulate perchlorate in our drinking water.

Please help!

Kelsey Ogburn 805 Redwood Trail Crownsville MD 21032

Response: See response to comment code 6120.

Commenter Name: William J. Shaw
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2157
EPA Comment ID: 22087
EPA Comment Code: 6120

Comment: Dear EPA,

I urge you to regulate the amount of perchlorate in our drinking water supply. This issue is vital to our future.

Sincerely, William J. Shaw 299 Aston Forest Ln Crownsville, MD 21032

Response: See response to comment code 6120.

Commenter Name: J Savage
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2158
EPA Comment ID: 22088
EPA Comment Code: 6120

Comment: Jomi Savage

We don't want harmful chemicals in our drinking water! They serve no usefull purpose and only impair our well being. So please for god sake, STOP PUTTING THAT [expletive] IN OUR WATER!!

Thank you.

Response: See response to comment code 6120.

Commenter Name: Gary Elson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2159
EPA Comment ID: 22089
EPA Comment Code: 6120

Comment: November 13, 2008

Water Docket, EPA Mailcode 2822T 1200 Pennsylvania Avenue Washington, DC 20460

Attn: Docket ID# EPA-HQ-OW-2008-0692

I support the regulation of perchlorate in drinking water and the strict enforcement of its prohibition. Perchlorate contaminations is a nationwide problem and the protection of the public health requires such regulation on a nationwide basis.

Gary Elson 409 Kyle Rd. Crownsville, MD 21032

Response: See response to comment code 6120.

Commenter Name: Elaine & George Anderson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2160
EPA Comment ID: 22090
EPA Comment Code: 6120

Comment: 11/17/08

To: EPA Water Docket,

I am a Virginia voter, and a kayaker and interested in preserving our waters. Perchlorate is a dangerous chemical found in 37 states. Since it can get into water and children's thyroids are vulnerable, it needs to be regulated.

Elaine Anderson George Anderson

Response: See response to comment code 6120.

Commenter Name: Molly J. Hall
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2163
EPA Comment ID: 22093
EPA Comment Code: 6120

Comment: November 11, 2008

Dear EPA,

It is time you take the health and safety of our drinking water seriously. We need a federal law that will keep the chemical, perchlorate out of our drinking water.

Please move swiftly on this matter. The health and safety of your constituents depends on your quick action.

Molly J. Hall Arnold, MD

Response: See response to comment code 6120.

Commenter Name: Cather Pauly
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2164
EPA Comment ID: 22094
EPA Comment Code: 6120

Comment: Dear EPA,

From a concerned Virginia resident, as a hopeful mom to be, I urge you to reconsider your decision not to regulate perchlorates, which could potentially harm not only me and my pets, but also my future children. This is a serious matter for all of our health & welfare. Please help keep us safe.

Thank you Cather Pauly 3108 Wellington Rd Alexandria VA 22302

Response: See response to comment code 6120.

Commenter Name: Teresa Avery
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-2165
EPA Comment ID: 22095
EPA Comment Code: 6120

Comment: Dear EPA,

I urge you to regulate the amount of perchlorate in our drinking water supply.

Sincerely, Teresa Avery 1246 Timber Turn Arnold, Md. 21012

Response: See response to comment code 6120.

Commenter Name: Jean Sengelaub
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2166
EPA Comment ID: 22096
EPA Comment Code: 6120

Comment: To: EPA

I urge you to regulate the amount of perchlorate in our drinking water to a maximum of 2 ppb.

Sincerely, Jean Sengelaub 1289 Terrace Lane Arnold, MD 21012 11-10-08

Response: See response to comment code 6120.

Commenter Name: Jean Sengelaub
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2166
EPA Comment ID: 22097
EPA Comment Code: 6120

Comment: To: EPA

I urge you to regulate the amount of perchlorate in our drinking water to a maximum of 2 ppb.

Sincerely, Jean Sengelaub 1289 Terrace Lane Arnold, MD 21012 11-10-08

Response: See response to comment code 6120.

Commenter Name: Claire
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2167
EPA Comment ID: 22098
EPA Comment Code: 6120

Comment: EPA,

We all should have drinking water free of substances like perchlorate. Please take another look at regulation. Its impact could be more harmful than we know now - affecting the thyroid gland.

Thank you, Claire [illegible]

Response: See response to comment code 6120.

Commenter Name: Mark Milleker
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2168
EPA Comment ID: 22099
EPA Comment Code: 6120

Comment: Mark Milleker 112 Askewton Rd Severna Park MD 21146

Water Docket EPA Mailcode 2822T 1200 Pennsylvania Ave Washington, D.C. 20460

November 10, 2008

Re: Docket # EPA-HQ-OW-2008-0692

Not allowing the EPA to regulate perchlorate in drinking water makes no sense. Hopefully the Obama administration will overturn all executive orders that harm our environment and the people that drink water.

A national primary drinking water regulation is needed right away. Think of the cost savings we will achieve with a healthier population.

Make the right choice.

Mark Milleker Drinking Water Advocate 410 647-7264

Response: See response to comment code 6120.

Commenter Name: Jennifer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2169
EPA Comment ID: 22100
EPA Comment Code: 6120

Comment: November 12, 2008

Dear EPA,

I urge you to seriously consider regulating perchlorate in drinking water.

Sincerely, Jennifer [illegible] 211 St Andrews Road Severna Park, Md 21146

Response: See response to comment code 6120.

Commenter Name: Georgette A Irwin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2170
EPA Comment ID: 22221
EPA Comment Code: 6120

Comment: November 20, 2008

EPA -

Please work to regulate or eliminate PERCHLORATE from all drinking water.

Yours truly, Georgette A. Irwin 1044 Springhill Way Gambrills MD 21054 301-621-7881

Response: See response to comment code 6120.

Commenter Name: Bonita K Patterson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2171
EPA Comment ID: 22228
EPA Comment Code: 6120

Comment: Nov. 20, 2008

ATTN: EPA Water Docket

I am writing to ask you to please regulate perchlorate in drinking water.

This is a very harmful chemical and our water is already filled with plenty of other harmful chemicals.

I have lived in our house for 38 yrs. and had breast cancer 10 yrs. ago. We stopped using tap water @ that time. We now use reverse osmosis water filters.

I truly believe are water is one of the main reasons we have so much [illegible] in our development.

Listen to the people crying out for safe drinking water.

Bonita K. Patterson 867 Frost Valley Cir Gambrills, MD

Response: See response to comment code 6120.

Commenter Name:
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2173
EPA Comment ID: 22252

EPA Comment Code: 6120

Comment: 11-6-08

To whom it may concern,

Drinking water should be tested for perchlorate because children and adults could be harmed by these chemicals.

Thank you, (illegible)

Response: See response to comment code 6120.

Commenter Name: Rachelle Stanley
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2174
EPA Comment ID: 22323
EPA Comment Code: 6120

Comment: Water Docket EPA Mail code 2822T 1200 Pennsylvania Avenue Washington, DC 20460

ATTN: Docket ID No: EPA-HQ-OW-2008-0692

As someone who trusts the Government to protect me from "The Axis of Evil", I also trust that same Government to ensure I have safe, clean drinking water available to myself and my children. I recently learned that the EPA is intending to not regulate the amount of perchlorate in drinking water, and I find that frightening.

I strongly encourage you to reconsider this decision; as it will affect my two young children. Perchlorate has been linked to mental retardation, loss of hearing and speech or deficits in motor skills in children with thyroid problems. My children are genetically predisposed to thyroid disease, so this is very worrisome for me.

We have enough to worry about in this country: terrorism, education, health care, the economy, using less oil and reducing our carbon footprints. I don't want to have to worry about the water that crosses my children's lips too.

Sincerely, Rachelle Stanley 2607 April Dawn Way Gambrills, MD 21054

Response: See response to comment code 6120.

Commenter Name: Kaii Heward
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2175
EPA Comment ID: 22329
EPA Comment Code: 6120

Comment: 11/19/08

Dear Fellow American,

I am writing you concerning our water supply. Among all of the other contaminates in our drinking water, there is the issue of perchlorate and I hear the EPA does not intend to regulate this chemical. It is inconceivable to me that it is not already being monitored considering how it affects thyroids, motor skills, development and other kinds of mental health. It impacts our children the most. I feel that perchlorate should be part of the mandatory testing done for our water supply. The health of all American citizens is crucial. Basically, failure to remove perchlorate's effects is consciously neglectful. We need to lock after our own welfare and be our own advocates. Monies used to protect ourselves from this chemical are just that: Monies. Our health is priceless. Please vote to make the regulation of perchlorate mandatory for all states.

Thank you for your time,

Kaii Heward

Response: See response to comment code 6120.

Commenter Name: Carrie Allen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2176
EPA Comment ID: 22330
EPA Comment Code: 6120

Comment: My family and I would like the EPA to continue to regulate Perchlorate levels in our water supply. We have read that it can negatively affect our health in low levels.

Thank you Carrie Allen 2516 Vivaldi Ln Gambrills MD 21054

Response: See response to comment code 6120.

Commenter Name: Anna Hyde
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2177
EPA Comment ID: 22331
EPA Comment Code: 6120

Comment: To whom it may concern:

As a mother to be and the wife of a doctor, I am consistently troubled by what contaminants are contained in our drinking water, especially after several recent studies that have raised alarm. I urge you to reverse your decision and set a federal limit for perchlorate in drinking water. It can have disasterous health impacts, especially for infants and children.

Sincerely, Anna Hyde

Response: See response to comment code 6120.

Commenter Name: Andrea Leidolf
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2178
EPA Comment ID: 22332
EPA Comment Code: 6120

Comment: Nov 17, 2008

Dear epa,

I would like to see a limit set on perchlorate in drinking water.

Sincerely, Andrea Leidolf 909 N Overlook Dr Alexandria VA 22305

Response: See response to comment code 6120.

Commenter Name: Harrison B. Williams
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2179
EPA Comment ID: 22333
EPA Comment Code: 6120

Comment: To: the US Environmental Protection Agency

I strongly urge you to reverse your decision to NOT regulate perchlorate in drinking water. Because perchlorate does not readily dissipate and can contaminant drinking water for years after it is released into the environment, I believe it is imperative that it be regulated by the EPA.

Harrison B. Williams 3617 Oval Drive Alexandria, Va 22305

Response: See response to comment code 6120.

Commenter Name: Karl
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2180
EPA Comment ID: 22334
EPA Comment Code: 6120

Comment: 11/12/08

To All Concerned at the EPA:

Please keep perchlorate out of our drinking water.

If there are other solutions for getting rid of this please explore.

Thank you, Sincerely Karl Hutchinson 3761 Gunston Road Alexandria, VA 22302

Response: See response to comment code 6120.

Commenter Name: Kevin & Lita Yates
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2181
EPA Comment ID: 22335
EPA Comment Code: 6120

Comment: November 18, 2008

18801 Breeze Way Circle Olney, MD 20832

To Whom It May Concern:

We are very concerned about the EPA announcing its intention NOT to regulate perchlorate in drinking water. Perchlorate has been found in 37 states, and in public water systems serving over 20 million people. As parents of three growing children, we are especially concerned about the presence of perchlorate in our drinking water since it is a harmful chemical that can impair the thyroid gland, which controls growth, development and metabolism.

We need our government agencies to regulate harmful chemicals. This is the purpose of the EPA, to protect citizens from harmful pollution. Please protect the citizens of the United States by regulating the harmful chemical perchlorate in drinking water.

Thank you, Kevin and Lita Yates

Response: See response to comment ID 19873 under comment code 5220.

Commenter Name: Hillary Collyer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2182
EPA Comment ID: 22372
EPA Comment Code: 6120

Comment: 11/12/08

Dear EPA,

Perchlorate occurs widely. There are many sources of perchlorate contamination. Because there has not been routine testing, we do not know the full extent of contamination. I ask that you act quickly to perform appropriate tests and implement adequate regulation.

Thank you for your attention to this important matter.

Regards, Hillary Collyer 3775 Gunston Rd. Alexandria, VA 22302

Response: See response to comment code 6120.

Commenter Name:
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2183
EPA Comment ID: 22377
EPA Comment Code: 6120

Comment: EPA Washington, DC 20005

To Whom It May Concern:

Please address the issue of perchlorate in our DC drinking water, and protect us from the problems that can occur from over exposure. It is to that end that I fully endorse the efforts of the Clean Water Action organization and their efforts to rid our drinking water of this dangerous and harmful chemical.

Thank you for your interest in this matter.

Sincerely (illegible) 3507 Nst NW Was., DC 20005

Response: See response to comment code 6120.

Commenter Name: M. Jane Schumacher
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2185
EPA Comment ID: 22379
EPA Comment Code: 6120

Comment: Dear EPA,

Please regulate perchlorate because it impacts the health of children; fetuses, as well as adults.

The regulation of this substance in our drinking water is very important to me and to all others who are aware of this.

Please reconsider and make this an important regulation.

Thank you, M. Jane Schumacher

Response: See response to comment code 6120.

Commenter Name: Tina Carroll
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2189
EPA Comment ID: 22380
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

I am a concerned citizen of Maryland. I have recently learned of your decision to choose not to regulate perchlorate levels in our drinking water. In Maryland we have several known facilities that distribute perchlorate:

Aberdeen Proving Ground Alliant Tech Systems Naval Surface Warfare Center New Jersey Fireworks Thiokol Corporation

Response: This is not a comment, no response needed.

Commenter Name: Diego Bank
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2190
EPA Comment ID: 22383
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

I hope that our drinking water contaminants can be regulated, so that people aren't affected by the negative effects of perchlorate.

Thanks.

Sincerely, Diego Bank Kingston

Response: See response to comment code 6120.

Commenter Name: Brenda Lewis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2191
EPA Comment ID: 22390
EPA Comment Code: 6120

Comment: To All Readers,

Perchlorate is a harmful chemical found in our drinking water. It is used in Rocket fuel and explosives. Every day, citizens ingest thousands of gallons nationally. If something is not done soon, This great country will be left a barren wasteland with no humans to care for it and all our efforts will have been wasted. Perchlorate can cause massive problems both physically and mentally to any human that ingests it.

Response: This is not a comment, no response necessary.

Commenter Name: Brenda Lewis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2191
EPA Comment ID: 22392
EPA Comment Code: 6120

Comment: This country strives not on its technological booms, but the minds that drive them. If we do not act now, it'll soon be too late and what use will these technological advances be to us then. Without the bright minds of our citizens, what use is a government who wouldn't act when it had the chance.

If the EPA does not do something to prevent further problems now, then there is no point in allowing them to stay as a federal agency anymore. The EPA has a responsibility to act now and as such should proceed with all haste. No Bureaucratic procedure or code should stop them. No effort should be made to stop them from proceeding to fulfill their duty to this great country.

There are many sources of perchlorate contamination including many military bases, fireworks manufacturers, and blasting at construction sites. If there were more routine testing then perhaps the problem could be more properly identified. Currently perchlorate has been found in 37 states, and in public water systems serving over 20 million people.

Respectfully, Brenda Lewis

Response: See response to comment code 6120.

Commenter Name: James Kirk
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2192
EPA Comment ID: 22399
EPA Comment Code: 6120

Comment: To whom it may concern:

My family and I are greatly concerned that the EPA is considering not to regulate perchlorate in our drinking water.

We fully support a national primary drinking water regulation to protect future generations.

Thanks James Kirk 2482 Red Fall Ct Gambrills, MD 21054

Response: See response to comment code 6120.

Commenter Name: Leigh E
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2193
EPA Comment ID: 22408

EPA Comment Code: 6120

Comment: 11-20-08

Dear EPA

If you are truly an agency that protects the environment you will understand that perchlorate contamination is a nationwide problem and that it has health impacts at lower levels than previously thought.

Many people can not afford either bottle water or to filter their water. I have a thyroid problem. Could it be from drinking perchlorate? We need a national primary drinking water regulation to protect all of us.

Sincerely Leigh E [illegible]

Response: See response to comment code 6120.

Commenter Name: Georgia
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2194
EPA Comment ID: 22409
EPA Comment Code: 6120

Comment: Dear EPA Folks,

Perchlorate in the water is a terrible thing for our nation's children, and to think it's allowed in the DC water is awful. Please think about regulating this!

Thank you, Georgia [illegible] 3519 Prospect St NE Was., DC 2007

Response: See response to comment code 6120.

Commenter Name: Ben Richeda
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2204
EPA Comment ID: 22410
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

Seriously,

The US has the best drinking water in the world. I should know, I've been around. However, implicit in this assumption is the trust that the EPA is doing a good job. Don't mess this up for the rest of us who can't afford bottled water or filters.

Sincerely, Ben

Sincerely, Ben Richeda 1160 Camino Cruz Blanca Santa Fe, NM 87505

Response: See response to comment code 6120.

Commenter Name: Sarah Beth Cassel
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2205
EPA Comment ID: 22411
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

I think it is obvious to protect our future generations. My boyfriend is a father of a young one and and hope one day to be a mommy. I already have to worry about mercury levels in my fish... and now i have this to be concerned about. We are poisoning our earth and rightfully we are the ones paying for it, but protect the innocents. let us become a nation that is ecologically intelligent and looking into the future and no be so selfish. please.

Again, I urge you to reverse your decision and to set a national drinking water standard for perchlorate.

it is that important.

Sincerely,

Sarah Beth Cassel 115 N. Beechwood Ave. Catonsville, MD 21228

Response: See response to comment code 6120.

Commenter Name: Dixie Walker
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2210
EPA Comment ID: 22412
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

I urge you to set a drinking water standard for perchlorate. Perchlorate is found in drinking water in at least 26 states, and 20-40 million people could be exposed to this chemical. Businesses and Individuals appreciate "Standards" and "Standards for safe drinking water" is something the average U.S. citizen believes the EPA provides. They have no idea that the upmost is not being done to protect the countries supply of clean water. Do the right thing for the multitude of taxpayers who are busy making a living and raising a family. THEY TRUST that the EPA is looking out for their health - Honor their confidence in you by insuring that perchlorate is regulated throughout the U.S.A.

I urge you to reverse your decision and to set a national drinking water standard for perchlorate.

Sincerely, Dixie Walker 214 Chase Dr Pelham, AL 35124

Response: See response to comment code 6120.

Commenter Name: Anita Brightman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2211
EPA Comment ID: 22413
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

I urge you to set a drinking water standard for perchlorate. I live near Aberdeen Proving Ground and have countless friends who suffer with thyroid disease. While working on Post, I too was diagnosed with thyroid problems and took synthroid for 10 years. Once I stopped drinking that water and changed jobs, I could not get my thyroid regulated. They eventually took me off the medicine because my thyroid function was in normal ranges.

This is an important issue and warrants attention and more study.

Sincerely, anita brightman 210 archer street bel air, MD 21014

Response: See response to comment code 6120.

Commenter Name: Andrea Link
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2216
EPA Comment ID: 22415
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

I am writing to urge you to keep out water clean. It should be mandated that toxic chemicals be kept out of our water. There should be no question about this subject. Why on earth would you even consider not taking care of the health of our people?

Please keep our water clean.

Sincerely, Andrea Link 4028 S. Delaware Englewood, CO 80110

Response: This is not a comment, no response necessary.

Commenter Name: Andy Burgess
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2217
EPA Comment ID: 22416
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

I cannot believe you have decided not to set a drinking water standard for perchlorate that will protect pregnant women and babies nationwide.

There is no excuse for this decision - no financial, statistical, or political rationale can offset the moral obligation you have to protect the citizens of the USA from dangerous exposure to chemicals we recognize and understand how to abate.

Response: See response to comment code 6120.

Commenter Name: Andy Burgess
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2217
EPA Comment ID: 22418
EPA Comment Code: 6120

Comment: Again, I urge you to reverse your decision and to set a national drinking water standard for perchlorate.

Sincerely, Andrew Burgess 2615 6th Street Boulder, CO 80304

Response: See response to comment code 6120.

Commenter Name: Neil and Pam Ackerman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2219

EPA Comment ID: 22419
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

Keep perchlorate OUT of our drinking water, PLEASE!

Sincerely, Neil and Pam Ackerman 8500 Falmouth Ave #3313 Beachport Complex Playa Del Rey, CA 90293-8727

Response: See response to comment code 6120.

Commenter Name: Amy Geffre
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2223
EPA Comment ID: 22420
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

Hello.

As a student of toxicology and a mother, I urge you to set a drinking water standard for perchlorate that will protect pregnant women and babies nationwide. I know you must already understand the potential health problems perchlorate can cause, so I will not lecture, but please take note of what I say.

My son is just older than newborn; tap water goes into his formula and that of many other small children that I know and do not. Their nervous systems are fragile yet as they develop; when there is even the most minute chance of harming or stunting so precious a part of them, I feel that it is cause for strict, non-discriminate regulations to be put in place concerning such potentially harmful agents.

"Perchlorate is found in drinking water in at least 26 states, and 20-40 million people could be exposed to this chemical." This statement worries me. I see my son developing, making cause-and-effect relationships, beginning to comprehend color, beginning to respond to me with smiles. It makes me feel fulfilled beyond anything else I've felt. I can't imagine how horrible it would be for a mother to look at her child and know that her baby couldn't do such things because of exposure to a harmful chemical.

I am aware that the problem of this compound's presence in drinking water is not necessarily so bad as to cause such heavy retardation in a child, but I worry about the potential for the situation to fast

become as such, thus I write to you to consider making a blanket regulation preemptively to ensure drinking water will never have harmful levels of perchlorate.

Problems are best avoided by ensuring that they can't happen to begin with. Please consider this. I urge you to. Please reverse your decision and set a national standard on perchlorate. Children are depending on us to keep them safe and healthy. Let's not make them lose their faith in us.

Sincerely, Amy Geffre 131 N Clark St Apt. B Forest City, IA 50436

Response: See response to comment code 6120.

Commenter Name: Kim Leerdam
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2224
EPA Comment ID: 22421
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

Are you seriousssssssssssss??????????????????

Be logical.

Again, I urge you to reverse your decision and to set a national drinking water standard for perchlorate.

I hope Robert Kennedy Jr takes over the EPA and you all get fired for being so insincere.

Sincerely, Kim Leerdam 410 N. Rossmore Ave #405 Los Angeles, CA 90004

Response: See response to comment code 6120.

Commenter Name:
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2226
EPA Comment ID: 22422
EPA Comment Code: 6120

Comment: EPA Water Docket

I am a student and I'm studying Biology. Perchlorate is a dangerous chemical and in the water. We need to protect children so it must be regulated.

Sincerely, [illegible]

1721 Crestwood Dr. Alexandria, Va 22302

Response: See response to comment code 6120.

Commenter Name: Malcolm Herstand
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2227
EPA Comment ID: 22423
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

Please!

Set a limit for perchlorate levels in water.

Your report talks about doses over months. But people live and drink from their water supply for decades.

Maximum levels would be enforceable by encouraging reduction and containment of perchlorate use in fireworks and battery manufacturing.

As a hydrologist for Montana State, I understand that groundwater contamination is receiving increased attention, and citizens are becoming more educated about it.

Don't become known as the

Sincerely, Malcolm Herstand 1625 W. Kagy Bozeman, MT 59715

Response: See response to comment code 6120.

Commenter Name: Mary Miller
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2229
EPA Comment ID: 22424
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

I urge you to reverse your decision and to set a national drinking water standard for perchlorate. Protecting our drinking water is becoming a greater problem, and it needs to be addressed. I believe

we have an obligation to protect people, especially pregnant mothers and children from dangerous chemicals in the water.

Thank you.

Sincerely, Mary Miller 417 Akers Drive Wilmore, KY 40390

Response: See response to comment code 6120.

Commenter Name: Marie Maccabee
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2240
EPA Comment ID: 22425
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

I urge you to set a drinking water standard for perchlorate that will protect life here on earth. I think it is necessary for your agency to set a national standard that is based on the best available science and that will protect public health. It would be litterally insane and completely unhuman for this group of yours to ignore your own staff scientists' reasonings about the dangers of this chemical. Contrary to your claims, protecting the health of young children is indeed a "meaningful opportunity for health risk reduction."

Again, I urge you to reverse your decision and to set a national drinking water standard for perchlorate.

Sincerely, marie maccabee 103 woodside ave thurmont, MD 21788

Response: See response to comment code 6120.

Commenter Name: Tigris Powers
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2244
EPA Comment ID: 22426
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

Perchlorate should NOT be anywhere near our nation's pregnant women, infants, children, or our drinking water supply. It's difficult to believe that this is an issue that has to be questioned, when it poses a health threat to to 20-40 million people nation wide.

When the health of young children is being put to the test, aren't we better off being SAFE than sorry?

Perchlorate poses a risk for pregnant women, newborns and young children by interfering with thyroid hormone, which is critical for optimal development of the brain and nervous system.

Today 1 in 159 children are diagnosed with autism, a disorder that is directly related to the brain and nervous system. Could there be a connection? Is it worth risking? I don't think so.

Response: See response to comment code 6120.

Commenter Name: Rose Lernberg
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2246
EPA Comment ID: 22428
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

Please reverse your decision and set a national drinking water standard for perchlorate that will protect pregnant women and babies nationwide.

Perchlorate interferes with the thyroid hormone, which is critical for optimal development of the brain and nervous system. it is present in drinking water in at least 26 states, and 20-40 million people could be exposed to this chemical. This especially poses a risk for pregnant women, newborns and young children.

It is urgent that you set a national standard, based on the best available science, to protect public health. Several states have set standards or guidelines for perchlorate, but these vary widely. Your own staff scientists say that not regulating perchlorate means some infants and young children will receive unsafe levels of exposure. The current draft scientific analysis should undergo independent scientific peer review and be used as the basis for the regulation.

All Americans deserve healthy and clean drinking water.

Response: See response to comment code 6120.

Commenter Name: Anna Kovach
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2247
EPA Comment ID: 22476
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

I currently am working for a State Assemblywoman in New York. I have recently been doing alot of research about what goes into public drinking water, namely pharmecuticals. Along with these, which affect everything from microbacterium to small fish and amphibians, there are also a whole slew of chemicals from everywhere else too. Please make sure you regulate what goes into the water.

I don't want anything worse to happen to my planet!!!

I urge you to set a drinking water standard for perchlorate that will protect pregnant women and babies nationwide. Perchlorate poses a risk for pregnant women, newborns and young children by interfering with thyroid hormone, which is critical for optimal development of the brain and nervous system. Perchlorate is found in drinking water in at least 26 states, and 20-40 million people could be exposed to this chemical.

Again, I urge you to reverse your decision and to set a national drinking water standard for perchlorate.

Sincerely, Anna Kovach 124 Prospect Ave Apt 5 Binghamton, NY 13901

Response: See response to comment code 6120.

Commenter Name: Roman Berka
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2249
EPA Comment ID: 22477
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

Thanks for doing nothing about perchlorate - great job.

Signed, The American People

Sincerely, Roman Berka 1260 Hillside Vw Algonquin, IL 60102

Response: This is not a comment, no response necessary.

Commenter Name: Rhona Schwartz
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2251
EPA Comment ID: 22478

EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

For heaven's sakes, don't we have enough trouble with our imported food supply! What the heck is perchlorate doing in our water!

You're supposed to help keep Americans safe. Get perchlorate banned and banished before all hell breaks loose.

Sincerely, Rhona Schwartz 315 First Ave. W., #210 Seattle, WA 98119

Response: See response to comment code 6120.

Commenter Name: William McGhee
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2266
EPA Comment ID: 22479
EPA Comment Code: 6120

Comment: WILLIAM MCGHEE 5 ROSENEATH COURT OLNEY MD 20832

U.S. ENVIROMENTAL PROTECTION AGENCY

E.P.A. Please take time to reconsiders the announced intention not to regulate per chlorate into our water system. I personally think this could provide a problem not only to my self but also to my children and my neighbors children. I did grow up in a time when you could drink from a water hose, but it was from a well. I have had the problem with broken water lines pollute our water system enough, to make me want to pop a well in the city. Please look at all options to regulate my and my families drinking water, for the future of my children and yours.

Thank You, William Mcghee

Response: See response to comment code 6120.

Commenter Name: T., Craig, Sophie & Ian Brouillette
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2268
EPA Comment ID: 22480
EPA Comment Code: 6120

Comment: November 24, 2008

To the EPA:

As a mother of two small children and a firm advocate of drinking plenty of water every day, my family and I are deeply disturbed to hear that the EPA has decided NOT to regulate perchlorate in our drinking water.

Perchlorate contamination is a nationwide problem that must be addressed and remedied. The effects of unsafe levels of perchlorate on the thyroid gland currently known that can have adverse impacts on health are devastating.

We want the EPA to regulate perchlorate levels in our drinking water, and a Nation primary drinking water regulation is needed.

Sincerely, The Brouillette Family of Maryland [illegible] Craig Sophie Ian

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2269
EPA Comment ID: 22481
EPA Comment Code: 6120

Comment: EPA,

I don't think I have to highlight the importance of the environment and the effect it has on people and more important children and animals, so I write this letter to illustrate my passion for the welfare and health of all human when I say please lets learn from the past of ignorance and please test and regulate Perchlorate.

Respectfully, Concerned Citizen

Response: See response to comment code 6120.

Commenter Name: Glenn M. Phillips
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2270
EPA Comment ID: 22482
EPA Comment Code: 6120

Comment: November 24, 2008

Glenn M. Phillips 7778 Kidwell Dr. Hanover, MD 21076

Water Docket, EPA Mailcode 2822T 1200 Pennsylvania Ave. Washington, DC 20460

ATTN: Docket ID No. EPA-HQ-OW-2008-0692

To whom it may concern,

Perchlorate is harmful and needs to be regulated in our water supply. This is a nation-wide problem and carries health impacts to everyone. Please review your choice not to regulate perchlorate in drinking water and amend your decision, as is only proper.

Sincerely, Glenn M. Phillips

Response: See response to comment code 6120.

Commenter Name: Debbie
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2274
EPA Comment ID: 22483
EPA Comment Code: 6120

Comment: Dear EPA:

Perchlorate is harmful and needs to be tested in our water. Please take action to resolve the matter.

Debbie [illegible] 788 Sunny Chapel Rd Odento Md 21113

Response: See response to comment code 6120.

Commenter Name: Mary Ogburn
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2275
EPA Comment ID: 22484
EPA Comment Code: 6120

Comment: 11/13/08

EPA

You must continue to regulate perchlorate in our drinking water. Please help.

Mary Ogburn 805 Redwood Trail Crownsville MD 21032

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2276
EPA Comment ID: 22485
EPA Comment Code: 6120

Comment: Dear EPA,

Please regulate our drinking water. Help us keep our water safe and clean.

Response: See response to comment code 6120.

Commenter Name: Jessica Gillengerten
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2277
EPA Comment ID: 22486
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

hello.

i am curious about this disinterest in regulating national drinking water.

why wouldn't we want to continue to maintain healthy standards for our primary necessity in life?

i spent many years in quebec, and enjoyed the benefit of seeing the true sources of the water supplies to their entire city.

it's remarkable to note the difference, between florida sulphur water... carolina mountain water... new york city tap water... chicgao re-filtered lake michigan water...hawaiian lava rock filtered water, and canadian melted snow.

of course there are geographic differences that create natural filtration variances, but why should we be sacrificing anything when it comes to keeping our water clean?

we are capable of doing great things. we have boundless technology, and plenty of educated people looking to work...

why not set a noble task, and pursue excellent standards?

Perchlorate does not sound like a natural part of H20. and since my tap water does not come with a list of ingredients, save for a once a year particulate analysis, i would really prefer to know the EPA was doing a fine job keeping an eye on what was coming into my glass.

the japanese are doing incredible things with water filtration. and as i have said, i was also very impressed with the great effort the canadians have put into protecting the pristine sources of their drinking water.

why shouldn't we take pride in a precious commodity? last i heard, it was a costly item in jordan, where people were standing in line to get a limited amount of clean bottled water issued to them.

and we painfully pollute, and waste...when we have the ability to improve.

again, I urge you to reverse your decision and to set a national drinking water standard for perchlorate, and to raise our standards overall.

clean water is a deciding factor for where i choose to live in this world. it's amazing to think that it is something the EPA could possibly be taking for granted. thank you.

Sincerely, jessica gillengerten 3407 gerhardt st sarasota, FL 34237

Response: See response to comment code 6120.

Commenter Name: Linda Yow
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2293
EPA Comment ID: 22488
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

Please set a protective drinking water standard for perchlorate as required by the Safe Drinking Water Act, reversing EPA's preliminary regulatory determination and doing what is right. Our food and water supplies are widely polluted with perchlorate and its toxic effects are well known, so action on this problem is urgent.

Exposure to perchlorate in the U.S. population exceeds the reference dose set by EPA, so EPA needs to incorporate the protective methodology for the sake of the millions of U.S. families exposed to dangerous levels of perchlorate contamination.

Thank you for your attention.

Sincerely, Linda Yow Route 1 Box 1650 Glen Allen, MO 63751

Response: See response to comment code 6120.

Commenter Name: James Pierson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2296
EPA Comment ID: 24977
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

For the good of our country, it is critical for the EPA to set national standards, based on the best available science, to protect public health. The EPA's scientists have determined that your decision not to regulate perchlorate places some infants and young children above safe levels of exposure. The EPA's current draft scientific analysis should undergo independent scientific peer review and should be used as the basis for regulations relative to perchlorate.

I urge you to reverse your decision and to set a national drinking water standard for perchlorate.

Sincerely, James Pierson 1079 Yorktown Drive Charleston, SC 29412

Response: The Agency believes that further review by the National Research Council would unnecessarily delay regulatory decision making for perchlorate. Therefore, EPA is not, at present, planning to request additional NRC review of issues related to perchlorate. Instead, EPA is issued a notice in August of 2009 seeking comments on a broad range of alternative approaches to the interpretation of the scientific data relevant to a regulatory determination for perchlorate in drinking water.

EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Kraig Erickson
Commenter Organization: RMC Water and Environment (RMC)
EPA Document ID: EPA-HQ-OW-2008-0692-2299
EPA Comment ID: 24978
EPA Comment Code: 6120

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

I urge you to set a drinking water standard for perchlorate that will protect pregnant women and babies nationwide. Perchlorate poses a risk for pregnant women, newborns and young children by interfering with thyroid hormone, which is critical for optimal development of the brain and nervous system. Perchlorate is found in drinking water in at least 26 states, and 20-40 million people could be exposed to this chemical.

Several states have set drinking water standards or guidelines for this chemical, but these standards vary widely, so it is critical for the EPA to set a national standard that is based on the best available science and that will protect public health. The EPA's own staff scientists have determined that your decision not to regulate perchlorate places some infants and young children above safe levels of exposure. The EPA's current draft scientific analysis should undergo independent scientific peer review and should be used as the basis for the regulation.

Response: The Agency believes that further review by the National Research Council would unnecessarily delay regulatory decision making for perchlorate. Therefore, EPA is not, at present, planning to request additional NRC review of issues related to perchlorate. Instead, EPA is issued a notice in August of 2009 seeking comments on a broad range of alternative approaches to the

interpretation of the scientific data relevant to a regulatory determination for perchlorate in drinking water.

EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Roland
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2300
EPA Comment ID: 24981
EPA Comment Code: 6120

Comment: Dear EPA

Please regulate perchlorate. This is harmful to our drinking water.

Roland [illegible] 16 W. [illegible] Ave Alexandria, VA 22301

Response: See response to comment code 6120.

Commenter Name: J. Elizabeth Callis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2301
EPA Comment ID: 24982
EPA Comment Code: 6120

Comment: Dear EPA,

Please regulate perchlorate

Thank you for paying attention

J Elizabeth Callis 19 W. Caton Ave. Alexandria, VA. 22301

Response: See response to comment code 6120.

Commenter Name:
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2302
EPA Comment ID: 24983
EPA Comment Code: 6120

Comment: Dear EPA,

Please regulate perchlorate!

[illegible] 437 E Luray Ave Alexandria, VA

Response: See response to comment code 6120.

Commenter Name: Shannon O'Donnell
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2303
EPA Comment ID: 24984
EPA Comment Code: 6120

Comment: DEAR EPA,

PLEASE REGULATE PERCHLORATE & TOXINS. IT CAUSES BIRTH DEFECTS AND IT IS SOMETHING THAT CONCERNS ME.

SINCERELY, SHANNON O'DONNELL

Response: See response to comment code 6120.

Commenter Name:
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2304
EPA Comment ID: 24985
EPA Comment Code: 6120

Comment: Dear EPA,

Please regulate perchlorate in our water system. It is harmful to children and pregnant women.

Sincerely, [illegible] 2406 Sanford St. Alexandria, VA 22301

Response: See response to comment code 6120.

Commenter Name: Daisy and G. Hickson Howell
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2305
EPA Comment ID: 24986
EPA Comment Code: 6120

Comment: Dear Epa Water Docket

- please regulate perchlorate that harmful to children.

Daisy Howell G. Hickson 612 N [illegible] St Alexandria VA

Response: See response to comment code 6120.

Commenter Name: John
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2306
EPA Comment ID: 24987

EPA Comment Code: 6120

Comment: Dear EPA Water Docket,

Please regulate perchlorate.

Thanks,

John [illegible]

Response: See response to comment code 6120.

Commenter Name: Heidi Mayor
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2307
EPA Comment ID: 24988
EPA Comment Code: 6120

Comment: 3614 Jenifer St., NW Washington, DC 20015 November 21, 2008

Water Docket, EPA, Mailcode 2822T 1200 Pennsylvania Ave., NW Washington, DC 20460

Re: Docket ID No. EPA-HQ-OW-2008-0692

Dear Environmental Protection Agency:

I am writing to urge, beg and even cajole you to set a federal limit for percholate in drinking water. Percholate is a nationwide probmem with significant health impacts. While I am fortunate enough to be able to afford to pay money to filter my drinking water, I believe that clean drinking water is a fundamental right of every American, including those who cannot afford to spend extra money to obtain it. Please regulate percholate. We will be a healthier, wealthier and wiser nation for your efforts.

With kind regards, Heidi Mayor

Response: See response to comment code 6120.

Commenter Name: C. Foni Bissessar
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2308
EPA Comment ID: 24989
EPA Comment Code: 6120

Comment: Please regulate perchlorate It's harmful to children and the environment

C. Foni Bissessar 610 N. Ripley St. Alexandria, VA 22304

Response: See response to comment code 6120.

Commenter Name: Cam Schaedel
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2309
EPA Comment ID: 24990
EPA Comment Code: 6120

Comment: Dear EPA

Please regulate perchlorate to keep our water safe for children.

Sincerely, Cam Schaedel 5336 Thayer Ave. Alexandria, VA 22304

Response: See response to comment code 6120.

Commenter Name: Jeremiah Marsh
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2311
EPA Comment ID: 24992
EPA Comment Code: 6120

Comment: EPA Water Docket

Please regulate perchlorate, it harms kids in development.

Jeremiah Marsh Medical School Student Howard University

Response: See response to comment code 6120.

Commenter Name: Caroline Schaffer
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2312
EPA Comment ID: 24994
EPA Comment Code: 6120

Comment: November 24, 2008

Dear EPA Water docket

Please regulate perchlorate. It harms childrens development.

Caroline Schaffer 5347 Holms Run Parkway Alexandria VA 22304

Response: See response to comment code 6120.

Commenter Name: Thomas Blackwood
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2313

EPA Comment ID: 24995
EPA Comment Code: 6120

Comment: 11/21/08

EPA Water Docket

I am a virginia fisherman/voter and wish to declare perchlorate as a dangerous chemical with negative health effects, especially for children. Since it is widespread and gets into water it should be regulated.

Thomas Blackwood 801 Ramsey St Alex VA 22301

Response: See response to comment code 6120.

Commenter Name: David
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2314
EPA Comment ID: 24996
EPA Comment Code: 6120

Comment: 11/24/08

To EPA water docket

I'm a Virginia voter and supporter of Virginia environment. Perchlorate is a dangerous chemical found in thirty seven states and affects the health of children. Since it gets into water we must call for it to be regulated.

Sincerely, David [illegible] 4909 Rutland Pl. Alexandria, VA 22304

Response: See response to comment code 6120.

Commenter Name: Melanie
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2315
EPA Comment ID: 24997
EPA Comment Code: 6120

Comment: As a concerned member of our area & a voter I wish to see that perchlorate be regulated because it gets into water supplies & has negative health effects, especially for children.

Sincerely, Melanie [illegible] 602 [illegible] St. Alexandria VA 22308

Response: See response to comment code 6120.

Commenter Name: Robert A.
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-2316
EPA Comment ID: 24998
EPA Comment Code: 6120

Comment: 11/20/08

EPA Water Docket

I am a long term Virginia resident. Perchlorate is a dangerous chemical. Since it gets into water & harms children, it should be regulated.

Robert A. [illegible] 406 Highland Pl Alexandria, VA 22301

Response: See response to comment code 6120.

Commenter Name: David Uhl
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2317
EPA Comment ID: 24999
EPA Comment Code: 6120

Comment: 11/20/2008 David Uhl

Water Docket, EPA, Mailcode 2822T 1200 Penn. Ave NW Docket ID No. EPA-HQ-OW-2008-0692

To whom it may concern:

Given our current problems with deregulation, I urge the EPA to reverse its decision and set a federal limit for perchlorate in drinking water.

Sincerely David Uhl, MPA

Response: See response to comment code 6120.

Commenter Name: Under 13
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2318
EPA Comment ID: 25000
EPA Comment Code: 6120

Comment: Dear EPA

I would like it if you find a better way to clean the water and not harm it or other people. I wish you take this in consideration. We need at least one good thing to happen in the world right now. Start by removing perchlorate water.

(p.s. why are you trying to clean the water this way?) (good luck)

[comment from patron under the age of 13]

Response: See response to comment code 6120.

Commenter Name: Under 13
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2319
EPA Comment ID: 25001
EPA Comment Code: 6120

Comment: To whom it may concern,

I learned there is a horrible chemical in our world. This chemical is called Perchlorate. Perchlorate can affect the thyroid gland, which controls growth, development and metabolism. This is very harmful to children and babies. This chemical has been found in 37 states. Therefore, WE NEED TO KEEP PERCHLORATE OUT OF DRINKING WATER!!!!!! Please help us keep our water safe by keeping Perchlorate out of our drinking water!

Sincerely, [comment from patron under the age of 13]

Response: See response to comment code 6120.

Commenter Name: Under 13
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2321
EPA Comment ID: 25002
EPA Comment Code: 6120

Comment: To Whom it may concern:

I learned that chemicals are in our water. I want to grow up healthy and strong so can you please make a law to keep perchlorate out of our water.

from, [comment from patron under the age of 13]

Hi there Girls Rule!

Response: See response to comment code 6120.

Commenter Name: Under 13
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2322
EPA Comment ID: 25003
EPA Comment Code: 6120

Comment: Water Docket EPA Mail code 2822T 1200 Pennsylvania Avenue Washington, DC 20460 ATTN: Docket ID No: EPA-HQ-OW-2008-0692

My name is [comment from patron under the age of 13]. I am six. I want to drink clean water. My mom says I should write to you to tell you test for Perchlorate. She's usually right about that kind of stuff. Please reconsider your decision to not test for Perchlorate. My future depends on it.

Thank you, [comment from patron under the age of 13]

Response: See response to comment code 6120.

Commenter Name: Under 13
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2323
EPA Comment ID: 25004
EPA Comment Code: 6120

Comment: Dear EPA,

I think it is inportant to have clean water. Perchlorate should be filterd because it can inpair the thyroid gland. The thyroid gland controls groth, develope ment and metabolism. These prodlems are most likely to occur in kids like me. Please help us Fix this prodlem.

Thank you

Sincerely, [comment from patron under the age of 13]

Response: See response to comment code 6120.

Commenter Name: Under 13
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2324
EPA Comment ID: 25005
EPA Comment Code: 6120

Comment: Date 11/0/08

Dear EPA,

Please pass laws to keep perchlorate contamination out of our water. This is drinking water so we want to keep it clean. We don't want kids, parents, or babys to get sick. Also we don't want it to come to our water because we don't want our people to get sick too. So lets all try to keep our water CLEAN and save the people.

from, [comment from patron under the age of 13]

Response: See response to comment code 6120.

Commenter Name: Under 13
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-2325
EPA Comment ID: 25006
EPA Comment Code: 6120

Comment: November 21, 2008 [comment from patron under the age of 13]

Water Docket, EPA, Mailcode 2822T 1200 Pennsylvania Ave. NW Washington Dc 20460 Docket ID No. EPA-HQ-OW-2008-0692

To Whom It May Concern:

Please reverse your decision and set a federal limit for perchlorate in our drinking water. I may just be an 11 year old but I have a lot of years of water in my future so please protect my health and that of my families. Remember you drink and use this water too!

Kindly, [comment from patron under the age of 13]

Response: See response to comment code 6120.

Commenter Name: Under 13
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2326
EPA Comment ID: 25007
EPA Comment Code: 6120

Comment: 11/24/2008 [comment from patron under the age of 13]

To Whom it May Concern:

I urge you to reverse your decision and set a federal limit for perchlorate in drinking water. Perchlorate is a nationwide problem and has health impacts at lower levels than previously thought. Please protect public health, especially infants and children, by regulating perchlorate.

Sincerely, [comment from patron under the age of 13]

Response: See response to comment code 6120.

Commenter Name: Donna
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2328
EPA Comment ID: 25008
EPA Comment Code: 6120

Comment: 11/19/2008

To: EPA Water Docket

I am a Virginia voter and work supporting environmental organizations and issues.

Perchlorate is a dangerous chemical and is widespread in water supplies with especially negative effects in children. Therefore it is extremely important to see that it is regulated.

Sincerely, Donna [illegible] [illegible] W [illegible] Avenue Alexandria, VA 22301

Response: See response to comment code 6120.

Commenter Name: R. Travers
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2330
EPA Comment ID: 25010
EPA Comment Code: 6120

Comment: To EPA Water Docket

Please regulate perchlorate, it is harmful to most living things and doesn't belong in water.

R. Travers 432 E Luray Ave Alex. Va 22301

Response: See response to comment code 6120.

Commenter Name: Carl Wall
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2331
EPA Comment ID: 25011
EPA Comment Code: 6120

Comment: Attention EPA Water Docket,

I am extremely unhappy with the fact that perchlorate is an unregulated substance which pops up in water. This stuff can hurt children and in today's world we need to raise healthy Americans. Action needs to be taken so our country has safe standards.

Thanks, Carl Wall 513 E [illegible] Alex. VA 22301

Response: See response to comment code 6120.

Commenter Name: Emerson Tom
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2332
EPA Comment ID: 25012
EPA Comment Code: 6120

Comment: November 21, 2008 Emerso Tom 3615 Ingomar Place, NW Washington DC 20015

Water Docket, EPA, Mailcode 2822T 1200 Pennsylvania Ave. NW Washington Dc 20460 Docket ID No. EPA-HQ-OW-2008-0692

To Whom It May Concern:

Please reverse your decision and set a federal limit for perchlorate in our drinking water. I may just be a 13 year old but water is important to me and everyone I know. Please protect my health and that of my family. Remember you drink and use this water too!

Kindly, Emerson Tom

Response: See response to comment code 6120.

Commenter Name: Michelle
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2333
EPA Comment ID: 25013
EPA Comment Code: 6120

Comment: Dear EPA Water Docket

Please regulate perchlorate in our water systems. The DoD already has a substitute to keep rockets flying.

Regards Michelle [illegible] 542 E [illegible] Ave Alexandria, VA 22301

Response: See response to comment code 6120.

Commenter Name: Tracie
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2334
EPA Comment ID: 25014
EPA Comment Code: 6120

Comment: Dear EPA,

Please regulate toxins from rocket fuel. They are harmful to children.

Thanks, Tracie [illegible]

Response: See response to comment code 6120.

Commenter Name: Dennis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2335
EPA Comment ID: 25015
EPA Comment Code: 6120

Comment: Nov. 20, 2008

Water Docket, EPA, Mailcode 2822T 1200 Pennsylvania Av, NW Washington, DC 20460 Docket ID No. EPA-HQ-OW-2008-0692

To whom it may concern:

Please reverse your recent decision on perchlorate in drinking water by setting a federal limit.

Perchlorate is a national problem that requires a Federal solution.

Sincerely, Dennis Stout

Response: See response to comment code 6120.

Commenter Name: M.L. Lang
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2336
EPA Comment ID: 25016
EPA Comment Code: 6120

Comment: To EPA

Regards perchlorate - absolutely not to be dumped in our waters. Please encourage known substitute for rocket fuel.

M.L. Lang 14 W. Rosemont Ave.

Response: Perchlorate is not being dumped into our waters.

Commenter Name: Under 13
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2338
EPA Comment ID: 25018
EPA Comment Code: 6120

Comment: 11/24/2008 [comment from patron under the age of 13]

To Whom it May Concern:

I urge you to reverse your decision and set a federal limit for perchlorate in drinking water. Perchlorate is a nationwide problem and has health impacts at lower levels than previously thought. Please protect public health, especially infants and children, by regulating perchlorate.

Sincerely, [comment from patron under the age of 13]

Response: See response to comment code 6120.

Commenter Name: Under 13
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-2339
EPA Comment ID: 25019
EPA Comment Code: 6120

Comment: Dear E.P.A,

I want clean drinking water. Please help all states provide their citizens with clean drinking water. I don't want people getting sick.

Sincerely, [comment from patron under the age of 13]

Response: See response to comment code 6120.

Commenter Name: Under 13
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2340
EPA Comment ID: 25020
EPA Comment Code: 6120

Comment: To Whom it may concern

There are bad chemicals in our water. Please make a law that keeps perchlorate out of the water so we can grow up healthy and strong.

From [comment from patron under the age of 13]

Response: See response to comment code 6120.

Commenter Name: Under 13
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2320
EPA Comment ID: 25036
EPA Comment Code: 6120

Comment: Water Docket EPA Mail code 2822T 1200 Pennsylvania Avenue Washington, DC 20460 ATTN: Docket ID No: EPA-HQ-OW-2008-0692

My name is [comment from patron under the age of 13] and I am three. I want to drink clean water just like my brother. My mom says I should write to you to tell you test for Perchlorate. She's usually right about that kind of stuff. Please reconsider your decision to not test for Perchlorate. My future depends on it.

[comment from patron under the age of 13]

Response: See response to comment code 6120.

Commenter Name: Olivia Butler
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-2329
EPA Comment ID: 25037
EPA Comment Code: 6120

Comment: Dear EPA Water Docket

Please regulate perchlorate it's harmful to children, and can be replaced with other chemicals for rocket fuel.

Olivia Butler 423 E Juray Ave Alexandria, Va. 22301

Response: See response to comment code 6120.

Commenter Name: T.C. Nelson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2341
EPA Comment ID: 25038
EPA Comment Code: 6120

Comment: Dear EPA

Please regulate perchlorate - it is dangerous to our family and future

Sincerely, T.C. Nelson 15 W. [illegible] Alexandria VA 22301

Response: See response to comment code 6120.

Commenter Name: Julia Goldstein
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2342
EPA Comment ID: 25039
EPA Comment Code: 6120

Comment: Dear EPA,

Perchlorate is bad for people to consume. Limits should be set on how much is in our drinking water source.

Julia Goldstein 4201 Massachusetts Ave, NW 8008E Washington, DC 20016

Response: See response to comment code 6120.

Commenter Name: Diane Millard
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2343
EPA Comment ID: 25040
EPA Comment Code: 6120

Comment: Diane Millard 3503 Valley Dr. Alexandria, VA 22302

Dear EPA;

Please ban/regulate perchlorates in the drinking water in the DC/Northern VA area. These chemicals have been proven to cause disabilities in children, specifically affecting the thyroid.

Please take the action to rid this toxic pollutant from our water and environment. I and generations to follow will greatly appreciate that action be taken now.

Sincerely, Diane Millard

Response: See response to comment code 6120.

Commenter Name: JoAnn Tom
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2344
EPA Comment ID: 25041
EPA Comment Code: 6120

Comment: November 21, 2008 JoAnn Tom 3615 Ingomar Place, NW Washington DC 20015

Water Docket, EPA, Mailcode 2822T 1200 Pennsylvania Ave. NW Washington Dc 20460 Docket ID No. EPA-HQ-OW-2008-0692

To Whom It May Concern:

Please reverse your decision and set a federal limit for perchlorate in our drinking water. Please protect our health and that of our families. Remember you drink and use this water too!

Kindly, JoAnn Tom

Response: See response to comment code 6120.

Commenter Name: Joan Kennan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2345
EPA Comment ID: 25042
EPA Comment Code: 6120

Comment: November 10, 2008

Water Docket, EPA Mailcode 2822T 1200 Pennsylvania Ave. Washington, DC 20460

ATTN: Docket ID No. EPA-HO-OW-2008-0692

In reference to EPA's intention not to regulate perchlorate in drinking water, I urge you to reconsider this position:

Perchlorate can impair the thyroid gland which controls growth, development and metabolism. These impacts are especially harmful to children and fetuses.

I do believe that a national primary drinking water regulation is needed to protect public health.

Sincerely, Joan Kennan 3143 O Street, NW Washington, DC 20007

Response: See response to comment code 6120.

Commenter Name: Teresa Kelley
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2346
EPA Comment ID: 25043
EPA Comment Code: 6120

Comment: To whom it may concern,

I am writing to keep perchlorate out of my drinking water.

This is a problem for everybody including elderly, children and pets, also it can cause problems for people taking medications, like my family.

Please take this letter into consideration when you vote on this subject.

Thank you, Teresa Kelley 3109 Holly St. Alexandria, VA 22305

Response: See response to comment code 6120.

Commenter Name: Deborah Classman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2347
EPA Comment ID: 25044
EPA Comment Code: 6120

Comment: To: Water Docket, EPA, Mailcode 2822T 1200 Penn. Ave NW Washington DC 20460 Docket ID No EPA-HQ-OW-2008-0692

From: Deborah Classman 5240 Nebraska Ave NW Washington DC 20015

Nov. 21, 2009

Please reverse your decision to set a federal limite for perchlorate in drinking water. This chemical had deleterious effects on national health, even in very small amounts. Your job is to protect public health. Please do so and regulate perchlorate.

Deborah Classman

Response: See response to comment code 6120.

Commenter Name: Joseph (illegible)
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2348
EPA Comment ID: 25045
EPA Comment Code: 6120

Comment: Dear Department of Environmental Protection,

As an uncle of 13 children and a father-to-be I find it at the minimum troubling, and at most a travesty of justice that your body has decided not to regulate perchlorate in drinking water. It has been brought to my attention that even low levels of this chemical can have adverse health effects. The lack of care and disregard for what is right, good, and just, I find personally appalling. I propose that you and your body seriously reexamine your policies and your morals. I thank you for your time and courtesy in hearing me voice my complaints. I trust that in the end you will make the right decision.

Yours truly, Joseph [illegible] M.D.

Response: See response to comment code 6120.

Commenter Name: Wesley Thomas
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2349
EPA Comment ID: 25046
EPA Comment Code: 6120

Comment: EPA Water Docket

Perchlorate, a substance found in solid rocket fuels has no place in water. This substance needs to be kept out of the environment in order that it not stunt the growth of children like my daughter Victoria.

Wesley Thomas 405 East Luray Avenue Unit A Alexandria, VA 22301-1603 (202) 412-2926

Response: See response to comment code 6120.

Commenter Name: Enn Ki Janz
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2350
EPA Comment ID: 25047
EPA Comment Code: 6120

Comment: Dear EPA Water Docket

Please regulate perchlorate. Harms children development

Enn Ki Janz 5331 Holmes Run Pkwy Alexandria VA 22304

Response: See response to comment code 6120.

Commenter Name: Mary Cianningin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2351
EPA Comment ID: 25048
EPA Comment Code: 6120

Comment: EPA Water

Please regulate perchlorate its a harmful substance.

Mary Cianningin 540 E. Luray Ave. Alexandria, VA 22301

Response: See response to comment code 6120.

Commenter Name: Mary Cianningin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2351
EPA Comment ID: 25049
EPA Comment Code: 6120

Comment: EPA Water

Please regulate perchlorate its a harmful substance.

Mary Cianningin 540 E. Luray Ave. Alexandria, VA 22301

Response: See response to comment code 6120.

Commenter Name:
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2352
EPA Comment ID: 25050
EPA Comment Code: 6120

Comment: EPA:

PLEASE REGULATE PERCHLORATE - IT IS A HARMFUL SUBSTANCE.

[illegible] 10 E. Rosemont Alex, VA 22301

Response: See response to comment code 6120.

Commenter Name: Selma Munden
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2008-0692-2353
EPA Comment ID: 25051
EPA Comment Code: 6120

Comment: EPA Water Docket

Please regulate perchlorate its a harmful substance.

Selma Munden 508E Luray Ave. Alexandria, VA 22301

Response: See response to comment code 6120.

Commenter Name: Christine Kulinski
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2354
EPA Comment ID: 25052
EPA Comment Code: 6120

Comment: DEAR EPA REPRESENTATIVE -

PLEASE ENSURE OUR CITIZENS ARE NOT EXPOSED TO PERCHLORATE IN OUR WATER.

THANK YOU, CHRISTINE KULINSKI

Response: See response to comment code 6120.

Commenter Name: Leslie Durs
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2355
EPA Comment ID: 25053
EPA Comment Code: 6120

Comment: Dear EPA representative,

Please ensure our children are not exposed to perchlorate in our waters.

Thank you, Leslie Durs 128 E Rosemont Ave Alexandria VA 22301

Response: See response to comment code 6120.

Commenter Name: Jeannie Sharp
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2356
EPA Comment ID: 25054
EPA Comment Code: 6120

Comment: Dear EPA,

Perchlorate is a dangerous chemical and I believe we should set a limit on it.

Jeannie Sharp 906 N. Overlook Dr. Alexandria, VA 22305

Response: See response to comment code 6120.

Commenter Name: Avis Rana
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2357
EPA Comment ID: 25055
EPA Comment Code: 6120

Comment: Portland, Oregon November 4, 2008

Environmental Protection Avenue NW Washington DC 20460

Re: Docket EPA-HQ-OW-2008-0692 Drinking Water Preliminary Regulatory Determination

This letter is to request that your agency set a drinking water standard for perchlorate, consistent with the legislation endorsed by the Senate Environment and Public Works Committee, and that you monitor levels of the chemical in tap water.

Perchlorate is a chemical in rocket fuel that has been linked to thyroid problems in pregnant women, newborns and young children. The maximum safe level now established in drinking water is 15 times higher than what the EPA declared safe in 2002. Under this new standard, more than 16 million Americans would be exposed to unsafe levels of perchlorate in their drinking water, placing more than 16 million Americans at risk. Perchlorate has been found in the drinking water in 35 states in the U.S.

I hope you will set a federal standard establishing safe levels for perchlorate in drinking water and will make provision for monitoring which will assure that Americans can be assured their drinking water is free from this dangerous chemical.

Sincerely, Avis Rana

Response: See response to comment code 6120.

Commenter Name: Laura Milleker
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2358
EPA Comment ID: 25056
EPA Comment Code: 6120

Comment: Laura Milleker 112 A Askewton Rd S.P., M.D. 21146

Water Docket EPA Mailcode 2822T 1200 Pennsylvania Ave. Washington, D.C. 20460

Re Docket ID No. EPA-HQ-OW-2008-0692

I am writing to voice my strong opposition to not put regulations on perchlorate in drinking water. Perchlorate contamination is a nationwide problem. A national primary drinking water regulation is needed to protect public health.

Sincerely, Laura Milleker

Response: See response to comment code 6120.

Commenter Name: Kathryn L. Jacobson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2359
EPA Comment ID: 25057
EPA Comment Code: 6120

Comment: Kathryn L. Jacobson 3306 Holly Street Alexandria, VA 22305

Water Docket Environmental Protection Agency Mailcode 2822T 1200 Pennsylvania Avenue Washington, D.C. 20460

ATTN: Docket ID No. EPA-HQ-OW-2008-0692

To Whom It May Concern:

I am writing regarding percholate contamination, which is a nationwide problem and has health impacts at lower levels than previously thought. Please reverse your previous decision and provide a national primary drinking water regulation to prevent percholate contamination and protect the public health.

Thank you for your attention.

Sincerely, Kathryn Jacobson

Response: See response to comment code 6120.

Commenter Name: Leslie
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2360
EPA Comment ID: 25058
EPA Comment Code: 6120

Comment: 11/24/08

To EPA Water Docket,

I am a Virginia voter. Perchlorate is a dangerous chemical found in 37 states. It gets into water and effects the health of children, so it should be regulated.

Sincerely, Leslie [illegible] 602 N. Pickett St Alexandria, Va 22304

Response: See response to comment code 6120.

Commenter Name: Lewis Tara
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2363
EPA Comment ID: 25059
EPA Comment Code: 6120

Comment: EPA Water Docket,

Please regulate perchlorate! I have two young girls and would love to know that our water is as safe as possible!

Sincerely, Tara Lewis 522 E Luray Ave Alexandria, VA 22301

Response: See response to comment code 6120.

Commenter Name:
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2364
EPA Comment ID: 25060
EPA Comment Code: 6120

Comment: Dear EPA

Please regulate perchlorate. This is a harmful substance with known substitutes.

[Illegible] 12 W. Rosemont Ave Alexandria, VA 22301

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0036
EPA Comment ID: 28336
EPA Comment Code: 6120

Comment: I support EPA including Perchlorate on the National Primary Drinking Water List. I am especially concerned that it is not included to date as a pregnant woman. Small changes in maternal thyroid hormone levels during pregnancy have been associated with reduced IQs in children and high levels of perchlorate in the water could lead to mental retardation in children of mothers who consumed contaminated water. This is not just a health concern for fetuses and infants, but for anyone in our country suffering any kind of thyroid problems. Which considering how unhealthy Americans are, there are probably plenty of people who suffer from thyroid issues. Perchlorate allowed in the drinking water will only decrease the health of our population.

California has already taken steps to regulate this contaminant, EPA should too. EPA guideline of 1 part per billion for its public drinking water standard should be enforceable, not just a recommendation. EPA should be protecting human health and the environment, not industry. I sincerely hope and pray that EPA will go back to its mission statement and ignore industry influences. Fight for us and the environment, regulate Perchlorate in the drinking water today!

Response: See response to comment code 6120.

Commenter Name: W. Cucinotta
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0038
EPA Comment ID: 28339
EPA Comment Code: 6120

Comment: d. EPA should regulate all exposures from these types of chemicals as we know little about the harm they cause when exposed to or mixed with different medicines or the multiple other chemicals in our bodies or in individual water systems. Because there is not enough data about our exposures to these chemical "soups" to assure protection for the American people and until there is more data assuring our safety from mixing perchlorates with other drugs and chemicals, EPA should aim to control all exposure.

Response: See response to comment code 6120.

Commenter Name: Kathryn Taylor
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0041
EPA Comment ID: 28340
EPA Comment Code: 6120

Comment: Please consider our lives and our health and set a reasonable limit to perchlorate in drinking water. Our lives and our future depend on you. Don't be swayed by those with money and power. You are in your position to protect others.

Sincerely, Kathryn Taylor

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0043
EPA Comment ID: 28341
EPA Comment Code: 6120

Comment: I live in NJ and already face a multitude of pollution issues, so I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

Response: See response to comment code 6120.

Commenter Name: Deborah Roney
Commenter Organization: Clean Water Action
EPA Document ID: EPA-HQ-OW-2009-0297-0045
EPA Comment ID: 28342
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate. Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought;

To assist in keeping down health care costs to our country, protecting infants and children against this polutant is critical. A national primary drinking water regulation would provide a unique pre-emptive opportunity to protect public health. One that our government is responsible to do.

Thank you for taking action to protect our health and our economy.

Deborah Roney

Response: See response to comment code 6120.

Commenter Name: L. Obara
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0051
EPA Comment ID: 28343
EPA Comment Code: 6120

Comment: PLEASE KEEP PERCHOLATE OUT OF OUR DRINKING WATER! WE RELY ON YOU TO SET HEALTHY STANDARDS FOR ALL OF US! Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

Response: See response to comment code 6120.

Commenter Name: A.J. Melman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0058
EPA Comment ID: 28344
EPA Comment Code: 6120

Comment: Please regulate Perechlorate in drinking water. It does not belong in our water and it is your mandate to protect citizens from contaminates in our public water supplies.

Response: See response to comment code 6120.

Commenter Name: C. Ernst

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0063
EPA Comment ID: 28345
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate. perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; protecting infants and children is critical. a national primary drinking water regulation would provide a meaningful opportunity to protect public health. Why limit perchlorate?

Perchlorate is a harmful chemical that EPA claims has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher. Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills

Response: See response to comment code 6120.

Commenter Name: Beth Appelbaum
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0064
EPA Comment ID: 28346
EPA Comment Code: 6120

Comment: Please take perchlorate out of our drinkiing water! I already have thyroid issues and do not need any other problems nor want youing children to have issues. beth appelbaum

Response: See response to comment code 6120.

Commenter Name: Toula J. Halperin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0066
EPA Comment ID: 28347
EPA Comment Code: 6120

Comment: I urge the EPA to limit Perchlorate to 1 part per billion in our drinking water. This is especially important for the health and well being of young children. Yours sincerely, Toula J. Halperin 18 Watchung Road Short Hills, NJ 07078

Response: See response to comment code 6120.

Commenter Name: Samuel Fuller
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0071
EPA Comment ID: 28348
EPA Comment Code: 6120

Comment: Dear EPA

Your job is to protect US citizens- and the environment. Given the article in today's Sunday NY Times your incompetence and inertia is inexcusable. Please wake up to the tragedy before you and ban rocket fuel from our drinking water.

Fr Samuel Fuller

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0072
EPA Comment ID: 28349
EPA Comment Code: 6120

Comment: Being a student of the medical field I can tell you that perchlorate must be limited and should NOT be in our drinking water in random amounts! Please take whatever actions necessary to limit this highly effective and in large amounts, toxic substance in our country's drinking water supply.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0074
EPA Comment ID: 28351
EPA Comment Code: 6120

Comment: I believe we need to set a limit on the allocated amount of perchlorate in our country's drinking water. This chemical/ compound in known to be harmful to humans if ingested. We can not allow this problem to persist into the waters of our united states citizens any longer.

Response: See response to comment code 6120.

Commenter Name: J. Nadeau
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0086
EPA Comment ID: 28352
EPA Comment Code: 6120

Comment: Keep perchlorate out of my drinking water!

Response: See response to comment code 6120.

Commenter Name: Robert J. O'Connell
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0092

EPA Comment ID: 28354
EPA Comment Code: 6120

Comment: To Whom It May Concern: Please take action to STOP PERCHLORATE from entering our water systems. Recent studies seem to indicate that the threshhold levels at which serious harm to a fetus and onset of mental retardation, among other dangers, are lower than the originally predicted. Thank you for all you do to protect our health and our environment. Yours truly, Robert J.O'Connell

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0097
EPA Comment ID: 28355
EPA Comment Code: 6120

Comment: No rocket fuel in our drinking water!!

Response: See response to comment code 6120.

Commenter Name: B. Beckel
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0112
EPA Comment ID: 28356
EPA Comment Code: 6120

Comment: Please set a minuscule amount of Perchhlorate allowable in our drinking water. We believe reports that indicate many health problems and especially effects on the unborn from exposure to small amounts of Perchlorate. Now is the time for us to take charge of how our societal penchant for war and the profits of war affect our environment.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0113
EPA Comment ID: 28357
EPA Comment Code: 6120

Comment: A national primary drinking water regulation would send a message to the rest of the world that the United States practices what it preaches, but more importantly woul dprotect this country's citizens. Therefore I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

Response: See response to comment code 6120.

Commenter Name: L. Touzeau

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0121
EPA Comment ID: 28359
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate. perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; protecting infants and children is critical.a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Why limit perchlorate? Perchlorate is a harmful chemical that EPA claims has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher.Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism.Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

Response: See response to comment code 6120.

Commenter Name: L. Kier
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0123
EPA Comment ID: 28360
EPA Comment Code: 6120

Comment: Please keep percholate out of our drinking water. It is afffecting my thyrois and my daughter's speech.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0127
EPA Comment ID: 28362
EPA Comment Code: 6120

Comment: Please,I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate. Do it for your children

Response: See response to comment code 6120.

Commenter Name: B. Harris
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0135
EPA Comment ID: 28364
EPA Comment Code: 6120

Comment: Please keep perchlorate out of our drinking water.

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #10 - Group Unidentified
EPA Document ID: EPA-HQ-OW-2009-0297-0039
EPA Comment ID: 28365
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought;

protecting infants and children is critical.a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Response: See response to comment code 6120.

Commenter Name: J. Capozzelli
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0088
EPA Comment ID: 28366
EPA Comment Code: 6120

Comment: The U.S. Environmental Protection Agency (EPA) has still not decided whether to set a drinking water standard, a limit for perchlorate, an ingredient in rocket fuel that is contaminating water nationwide. Perchlorate is a harmful chemical that the EPA claims has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher. Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills. I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than one part per billion for perchlorate because berchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought. A national primary drinking water regulation would provide a meaningful opportunity to protect public health.Thank you.

Response: See response to comment code 6120.

Commenter Name: Noreen P. Cullen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0136
EPA Comment ID: 28367
EPA Comment Code: 6120

Comment: Dear Sir/Madam;

Perchlorate has been shown to be dangerous to human health and should not be ingested by anyone, especially by children. We need to do everything we can to remediate the waters that currently contain perchlorate and do even more to prevent further intrusion of perchlorate into the waters in our country.

Noreen P. Cullen 30 Delmar Rd Glastonbury, CT 06033 noreen@faeryspirit.com

Response: See response to comment code 6120.

Commenter Name: D. Browder
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0140
EPA Comment ID: 28368
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate. - perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; protecting infants and children is critical. - a national primary drinking water regulation would provide a meaningful opportunity to protect public health. If perchlorate is affecting the thyroid as substantially as indicated, it could also be contributing to the obesity of our nation. It could be slowing down the metabolism for those who would otherwise burn calories much more easily but because of a chemical issue going on in their body, it is slowed down significantly.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0146
EPA Comment ID: 28369
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of NO parts per billion for perchlorate.

- perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; protecting infants and children is critical. - a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

I mean, think about it. This affects YOUR water too!

Response: See response to comment code 6120.

Commenter Name: Joe Parrish
Commenter Organization: US Environmental Watch
EPA Document ID: EPA-HQ-OW-2009-0297-0148
EPA Comment ID: 28370
EPA Comment Code: 6120

Comment: I very urgently ask the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

Perchlorate contamination is a nationwide problem and has health impacts at far lower levels than previously thought; without this protection, infants and children will be damaged.

Perchlorate in concentrations above 1 PPB will impair the thyroid gland, which controls growth, development and metabolism. Developing fetuses, infants and children with thyroid impairment will suffer mental retardation, loss of hearing and speech and deficits in motor skills.

A national primary drinking water regulation at 1 PPB for perchlorate is absolutely essential to protect public health.

Do not delay adopting this essential limit for perchlorate.

Sincerely, Dr. Joe Parrish US Environmental Watch 300 E. 56th Street Suite 2B New York, NY 10022

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0152
EPA Comment ID: 28371
EPA Comment Code: 6120

Comment: As one who individually and whose children have been severely negatively impacted by Agent Orange (Dioxin), I can not imagine how anyone could be persuaded to allow Perchlorate reach our drinking water.

Response: See response to comment code 6120.

Commenter Name: Susanne Emerick
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0155
EPA Comment ID: 28372
EPA Comment Code: 6120

Comment: It is time to pass safer water regs. Keep perchlorate out of our drinking water.

Susanne Emerick

Response: See response to comment code 6120.

Commenter Name: Albert A. Bartlett
Commenter Organization: University of Colorado at Boulder
EPA Document ID: EPA-HQ-OW-2009-0297-0161

EPA Comment ID: 28374
EPA Comment Code: 6120

Comment: Dear Friends,

Please do all you can to keep perchlorate out of the drinking water systems.

With thanks and best wishes, I am,

Sincerely yours, Albert A. Bartlett Professor Emeritus of Physics, University of Colorado at Boulder.

Response: See response to comment code 6120.

Commenter Name: Beth Robelia
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0162
EPA Comment ID: 28375
EPA Comment Code: 6120

Comment: To whom it may concern:

Please set a standard to limit perchlorate in water. Data indicates it is hazardous to human health and should not be consumed by children or pregnant women. Limiting consumption by setting limits seems the most prudent course of action.

Regards, Beth Robelia

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0168
EPA Comment ID: 28377
EPA Comment Code: 6120

Comment: No more than one part per billion of perchlorate in our drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0171
EPA Comment ID: 28378
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

Response: See response to comment code 6120.

Commenter Name: Patrick Iannone
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0172
EPA Comment ID: 28379
EPA Comment Code: 6120

Comment: Dear Sirs/Madams,

As an industrial research scientist, I urge the U.S. Environmental Protection Agency to adopt a drinking water standard of no higher than 1 part per billion for perchlorate.

As we've seen over the past decade or more, the lack of strict government oversight in critical areas (such as the public health, banking, etc) leads to abuses by large corporations. Please continue your role in protecting infants and children from contaminated drinking water.

Regards, Patrick Iannone, Ph.D 146 Davis Lane Red Bank NJ, 07701

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0173
EPA Comment ID: 28380
EPA Comment Code: 6120

Comment: I urge the Environmental Protection Agency to set the drinking water standard for perchlorate to no more than 1 part /billion.

Although there are a number of health concerns with this chemical, I am especially concerned about the mischief it causes in thyroid function. As a federal government, we can take on the expenses of life-long medical care or we can fulfill our preemptive responsibilities to protect American citizens from a lifetime of disability. Please be strong and say "no" to relaxed standards for Perc.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0174
EPA Comment ID: 28381
EPA Comment Code: 6120

Comment: I am a concerned citizen and would like to facilitate change in my world. I don't like being killed with pollution by people and companies that are taking advantage of all of us. I have zero tolerance for pollution, greed and ignorance! Please get help get our world livable again. Stop perchlorate in water.

Response: See response to comment code 6120.

Commenter Name: Linc Cole
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0175
EPA Comment ID: 28382
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

Linc Cole 120 Cutlass Ln Cudjoe Key, FL 33042

Response: See response to comment code 6120.

Commenter Name: Bob Vaughan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0178
EPA Comment ID: 28383
EPA Comment Code: 6120

Comment: please set a national limit on the amount of the harmful chemical perchlorate allowed in our nation's drinking water.

thank you, Bob Vaughan Tampa,Florida

Response: See response to comment code 6120.

Commenter Name: R. Van Aken
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0180
EPA Comment ID: 28385
EPA Comment Code: 6120

Comment: The continual revelations regarding chemicals in our drinking water suggest we err on the side of caution regarding permissible limits. As we know the effects this chemical has on human beings I urge you to set the limit as low as feasible to prevent serious the serious health problems possible from inadvertent consumption of this chemical.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0187
EPA Comment ID: 28386
EPA Comment Code: 6120

Comment: Please set a high standard for limiting this chemical in our drinking water.

Response: See response to comment code 6120.

Commenter Name: Maureen Lattimore
Commenter Organization: Robert Bair Services
EPA Document ID: EPA-HQ-OW-2009-0297-0195
EPA Comment ID: 28388
EPA Comment Code: 6120

Comment: We need stronger legislation on keeping our water clean. There is only so much water and every day there is more data about that fact showing up and letting us know that the situation is getting worse. Please take strong action to keep our drinking water free of Perchlorate and other hazardous chemicals.

Response: See response to comment code 6120.

Commenter Name: Peggi Sturmfels
Commenter Organization: New Jersey Environmental Federation (NJEF)
EPA Document ID: EPA-HQ-OW-2009-0297-0204
EPA Comment ID: 28389
EPA Comment Code: 6120

Comment: I am a program organizer for NJ Environmental Federation as well as a mom and grandmother.

My deep concern about perchlorate in our waterways is growing. Particularly in regards to NJ which is now becoming a superfort by combining FT Dix, Mcquire Air Force Base and Lakehurst Navel Air Station. As a results, military air traffic has increased from 8000 to 80,000 over Centerl Jersey, which is home to the headwaters of the Metedeconk and Toms River and the Kirkwood Cohansey aquifer that supply most of the drinking water for central and South Jersey. Added to that, this area is less than 50 miles in any direction from a major commercial airport.

Setting standards for perchlorate at one part per billion is the only reasonable action that can be taken protect the children and residents of this area. Sadly you may be too late.

Response: See response to comment code 6120.

Commenter Name: K. Cunningham
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0218
EPA Comment ID: 28391
EPA Comment Code: 6120

Comment: Gentlemen;

I have read for a number of years about the infiltration of perchlorate mostly from some federal (or Federal contractor) facilities through ground water or other discharges into surface waters. Perchlorate contamination is found (for example) in the Colorado River system and in irrigation and

domestic water supplies drawing on it. Many of the California vegetables which millions of Americans enjoy have some perchlorate contamination. People with some knowledge of chemistry often assume that perchlorate is, like sulfate, fairly inert and innocuous at low concentrations. However, I understand that there is evidence that perchlorate has effects on thyroid health, even at sub-ppm concentrations, and it is known that its bromine analog, bromate, is to be avoided due to its toxic effects at low concentrations (one of the reasons that ozonation is not a viable drinking water treatment when bromide ion is present). For these reasons, and because the sources of perchlorate contamination are fairly limited, I would ask that EPA begin to regulate this chemical more stringently in discharges and in drinking water supplies, perhaps down to the 1 ppb level in the latter. Thank you for your consideration of this opinion.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0223
EPA Comment ID: 28392
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; protecting infants and children is critical.

a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

5 years ago, I developed hypothyroidism. There is no family history of this. I know many others. I can't help but wonder if perchlorate in the water used to grow vegetables in the western U.S. states is partly responsible. At age 51, the health concerns for me are nothing compared to those of children exposed to this. Please take action to help protect our health. Thank You.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0234
EPA Comment ID: 28393
EPA Comment Code: 6120

Comment: Common sense dictates that we keep our water supplies clean of pollutants. Why is that so hard to commit to? Please keep perchlorate and other contaminants out of the water.

I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

Response: See response to comment code 6120.

Commenter Name: Nancy Kuecke
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0238
EPA Comment ID: 28417
EPA Comment Code: 6120

Comment: I strongly recommend setting a limit NOW on the amount of perchlorate allowed in our drinking water!

Thank you for your time and effort.

Nancy Kuecke

Response: See response to comment code 6120.

Commenter Name: Merryl Gladstone
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0245
EPA Comment ID: 28419
EPA Comment Code: 6120

Comment: As a mother and a concerned citizen, I am writing in support of regulations restricting perchlorate in America's drinking water. It is dangerous and not what we as American citizen deserve in our drinking water. Listen to the scientific evidence and do write by people NOT industry. You are our voice.

Response: See response to comment code 6120.

Commenter Name: Patricia McPeak-La Rocca
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0255
EPA Comment ID: 28420
EPA Comment Code: 6120

Comment: I am a Certified Nurse- Midwife, and I write on behalf on pregnant women, their unborn fetuses, babies, children, families and individual citizens,who do NOTwant the inclusion of any amount of perchlorate in our drinking water. We rely on the EPA to protect our water sources and prevent public health problems. This is a substance known to be harmful in the scientific literature. We must be willing to protect our most vulnerable citizens who are not yet of age: babies and children. This is also a case of The Precuationary Principal; safety must be proven and not assumed.

I urge the U.S. Environmental Protection Agency to move forward and limit the amount of perchlorate in water to no greater than 1 part per billion.

Sincerely, Patricia McPeak- La Rocca, CNM Amherst, MA

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0256
EPA Comment ID: 28421
EPA Comment Code: 6120

Comment: I urge you to set regulations banning perchlorate of concentrations higher than 1 part per billion in drinking water. Perchlorate (even in small amounts) is linked to thyroid damage, which, in fetuses and children, can lead to intelligence disability (mental retardation), loss of hearing and speech, or motor impairment. It is unconscionable to allow the levels or perchlorate in drinking water to go unpunished and untreated.

Response: See response to comment code 6120.

Commenter Name: Walter McClure
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0265
EPA Comment ID: 28422
EPA Comment Code: 6120

Comment: On August 19, the U.S. Environmental Protection Agency (EPA) requested public comments related to setting a limit for perchlorate in drinking water. Last year EPA appeared poised to announce that it would not set a limit but is now reviewing scientific and other information to make a decision about moving forward with a regulation now.

Why limit perchlorate. It is a harmful chemical that EPA claims has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher.

Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism.

Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

Response: See response to comment code 6120.

Commenter Name: Nancy T. Miller
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0266
EPA Comment ID: 28423
EPA Comment Code: 6120

Comment: I urge the EPA to set a standard on perchlorate of one part per billion to ensure safe drinking water for everyone. -- Nancy T. Miller, Winona MN

Response: See response to comment code 6120.

Commenter Name: Thomas Clark
Commenter Organization: Clark Chiropractic Health Center, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0267
EPA Comment ID: 28424
EPA Comment Code: 6120

Comment: We must keep this and so many other chemicals out of our drinking water. We must move ahead towards more pure water, not "tolerable" levels.

Thomas Clark, D.C. St. Petersburg, FL

Response: See response to comment code 6120.

Commenter Name: Kathryn C. Westman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0268
EPA Comment ID: 28425
EPA Comment Code: 6120

Comment: As a concerned citizen and registered nurse, I feel it is important for the US EPA to set a limit on Perchlorate in public drinking water, limiiting it to a standard of no higher than 1 part/billion.

We must protect the population - especailly children and infants- from the impairment on the thyroid gland that higher limits might cause. Please take this step to protect our public health.

Sincerely, Kathryn C. Westman 104 S. Harleston Dr. Pittsburgh, PA 15237

Response: See response to comment code 6120.

Commenter Name: Susan van Asch van Wyck
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0275
EPA Comment ID: 28427
EPA Comment Code: 6120

Comment: We cannot understand why you would want to allow ANY perchlorate in our drinking water!! It is no wonder so many millions of Americans die of cancer. We are all at risk every day because of lax governmental control, as we had during the Bush years. Please do not extend these dangers during the Obama administration. Thank you.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0281
EPA Comment ID: 28428
EPA Comment Code: 6120

Comment: please keep perchlorate out of our drinking water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0282
EPA Comment ID: 28429
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

Health impacts of perchlorate are well documented and present serious problems, especially in children and infants.

Another reason why I RO filter all my water. But not everyone does or can afford to do so.

Response: See response to comment code 6120.

Commenter Name: Karen Parelhoff
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0291
EPA Comment ID: 28431
EPA Comment Code: 6120

Comment: We need perchlorate-free drinking water. Please regulate this harmful chemical to no more than one parts to a billion for our drinking water. We look to you to take care of us and protect our health from harmful chemicals in our soil, water, and air.

Karen Parelhoff

Response: See response to comment code 6120.

Commenter Name: Elaine Kampmann
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0295
EPA Comment ID: 28432
EPA Comment Code: 6120

Comment: I can't really imagine why there is much to debate here. I don't know if the agency has gotten stuck in some bureacreatic muddle, but our drinking water is becoming more and more contaminated and is already non-potable in areas of my city because of tri-chlor, per-chlor, etc.

Keep it out of the water!!!!

Thank you, Elaine Kampmann 2531 Wilkinson Rd. Sarasota FL 34231

Response: See response to comment code 6120.

Commenter Name: Pamela Hosler
Commenter Organization: Hawthorn Children's Psychiatric Hospital, Missouri Department of Mental Health
EPA Document ID: EPA-HQ-OW-2009-0297-0307
EPA Comment ID: 28435
EPA Comment Code: 6120

Comment: I urge the U.S. EPA to set a national limit on perchorlate in drinking water. It has been found in the public water systems that serve 20 million people. Small amounts affect the thyroid gland, which, in turn, can cause health problems.

A national standard allowing no more than 1 ppb perchorlate in drinking water would prevent many many health problems.

Response: See response to comment code 6120.

Commenter Name: Mark Knight
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0309
EPA Comment ID: 28437
EPA Comment Code: 6120

Comment: I urge EPA to move forward with an appropriate drinking water standard for perchlorate. The reason is simple: Perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; protecting infants and children is critical.

Mark Knight Arlington, VA

Response: See response to comment code 6120.

Commenter Name: Linda Jeub
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0316
EPA Comment ID: 28438
EPA Comment Code: 6120

Comment: The U.S. Environmental Protection Agency must move forward to protect our drinking water with a standard of no higher than 1 part per billion for perchlorate. How rocket fuel gets into our drinking water is beyond me.

From what I have heard, perchlorate contamination is showing up nationally, and has health impacts at lower levels than previously thought putting infants and children at risk.

We are at a point in our environmental history that requires paying attention to the basics and drinking water is about as basic as it gets. A national primary drinking water regulation would be a meaningful step in protecting public health.

Thank you, Linda Jeub

Response: See response to comment code 6120.

Commenter Name: Robert H. Michels
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0317
EPA Comment ID: 28439
EPA Comment Code: 6120

Comment: Please do not allow perchlorate into the drinking water in this country!!

Sincerely, Robert H. Michels 917-991-1367 rmichels57@yahoo.com

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0318
EPA Comment ID: 28440
EPA Comment Code: 6120

Comment: Please ensure that perchlorate is kept put of our drinking water. This is critical.

Response: See response to comment code 6120.

Commenter Name: Greg Black
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0320
EPA Comment ID: 28442
EPA Comment Code: 6120

Comment: About proposed regulations on Perchlorate in our water:

I am adamantly oppsed to allowing this chemical to continue to be dumped into my water. The U.S. Environmental Protection Agency should enforce a drinking water standard of no higher than 1 part per billion for perchlorate (I would prefer a more strick standard.).

Also, whant are we going to see some movement on Mercury Standards for coal powered plants?

We voted for change, and I want to see it now in EPS enforecement.

Most Sincerely,

Greg Black

Response: The issue of mercury standards for coal powered plants is outside the scope of this action. For your comment on perchlorate, see response to comment code 6120.

Commenter Name: Pauline DiBella
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0321
EPA Comment ID: 28443
EPA Comment Code: 6120

Comment: Nobody wants rocket fuel in their drinking water.

Why limit perchlorate????

- Perchlorate is a harmful chemical that EPA claims has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher. - Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. - Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

Sample Letter

I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

- perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; protecting infants and children is critical. - a national primary drinking water regulation would provide a meaningful opportunity to protect public health. Please act now to regulate perchlorate and protect our water supply.

thank you.

Pauline DiBella Devon, Pennsylvania

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0330
EPA Comment ID: 28444

EPA Comment Code: 6120

Comment: Please keep perchlorate out of drinking water. The safety of the public is vital!

Response: See response to comment code 6120.

Commenter Name: A. Crane
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0331
EPA Comment ID: 28445
EPA Comment Code: 6120

Comment: Let's keep our water safe! Please! I recently attended an Herbalists Festival and the attendance was double what the organizers had expected and many of the attendees were there to learn about caring for the lymphatic system. If it is proven and known that the perchlorate found in rocket fuel is bad for the thyroid and causes birth defects and has been found in 37 states then I hope and pray you get busy on regulating the presence of this chemical in our water ways, all of them - rivers, lakes, streams, wetlands and our city water systems. Who wants the rain to bring us cancer? I don't. Please work to stop the polluting, dumping and excess production of this hazardous substance. Thank you. Sincerely, A. Crane

Response: See response to comment code 6120.

Commenter Name: M. Dougherty
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0334
EPA Comment ID: 28446
EPA Comment Code: 6120

Comment: I am very concerned about Perchlorate contaminating our drinking water. Please set standards to eliminiated this threat to our health and the health of future generations.

Response: See response to comment code 6120.

Commenter Name: Damon J. Brinson
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0340
EPA Comment ID: 28448
EPA Comment Code: 6120

Comment: I am writing to urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

Perchlorate contamination of drinking water is a serious problem across our nation. The chemical impacts people's health at lower levels than previously thought. It is critical to protect infants and children from this toxic chemical.

I firmly believe that a federal drinking water regulation, with a standard of <= 1 PPB of perchlorate, would protect public health. Please support this standard.

Thank you, Damon J. Brinson 4860 Dona Lane Golden Valley, MN 55422

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0346
EPA Comment ID: 28450
EPA Comment Code: 6120

Comment: Nobody wants rocket fuel in their drinking water.

Response: See response to comment code 6120.

Commenter Name: R. Oliver
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0347
EPA Comment ID: 28451
EPA Comment Code: 6120

Comment: Nobody wants rocket fuel in their drinking water.

Perchlorate is a harmful chemical that EPA claims has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher.

Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

Response: See response to comment code 6120.

Commenter Name: R. Oliver
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0356
EPA Comment ID: 28453
EPA Comment Code: 6120

Comment: Nobody wants rocket fuel in their drinking water.

Perchlorate is a harmful chemical that EPA claims has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher.

Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

Response: See response to comment code 6120.

Commenter Name: G. Spring
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0361
EPA Comment ID: 28455
EPA Comment Code: 6120

Comment: Please. No perchlorate in our water. Water is life.

Response: See response to comment code 6120.

Commenter Name: K. Stote
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0366
EPA Comment ID: 28457
EPA Comment Code: 6120

Comment: Please don't allow perchlorate to be present in our drinking water without any limits, we need to set a maximum allowance amount. Do it for our future generations, cause once it's done, there's not a hell more we do to change it.

Thank you.

Response: See response to comment code 6120.

Commenter Name: W. Brunkhorst
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0375
EPA Comment ID: 28460
EPA Comment Code: 6120

Comment: The EPA has yet to set standards for perchorate,a component of aircraft fuel. It is critical to take action now,before perchlorate is detected in drinking water. Prevention is much cheaper than spending millions correcting a problem that is bound to occur.

Response: See response to comment code 6120.

Commenter Name: Susan Marie Frontczak
Commenter Organization: Storysmith
EPA Document ID: EPA-HQ-OW-2009-0297-0377

EPA Comment ID: 28461
EPA Comment Code: 6120

Comment: Thyroid impairment, mental retardation, loss of hearing and speech, and motor skill deficits are all problems that can result from perchlorate contamination of drinking water. While the health care reform debate rages, let's make some common sense choices so that fewer people need health care or disability income. I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

Response: See response to comment code 6120.

Commenter Name: Janice Church
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0378
EPA Comment ID: 28462
EPA Comment Code: 6120

Comment: Please make a scientific, not a political, decision regarding the allowable levels of percholate in our drinking water.

Your decision will impact your children, my children, and our grandchildren. Please make your decision based on the best scientific evidence available. Please leave politics out of your equation as best you can.

Thank you. Janice Church New Tennessee resident

Response: See response to comment code 6120.

Commenter Name: Michael Rice
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0386
EPA Comment ID: 28463
EPA Comment Code: 6120

Comment: * Perchlorate is a harmful chemical that EPA claims has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher. * Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. * Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

* perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; protecting infants and children is critical. * a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Thank you for hearing my concerns Sincerely, Michael Rice

Response: See response to comment code 6120.

Commenter Name: Jeff Franklin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0388
EPA Comment ID: 28464
EPA Comment Code: 6120

Comment: Dear EPA,

Please make our water safe from Perchlorate. NO amount is truly safe. Please think about your children and grandchildren drinking the water you approve.

Be well, Jeff Franklin 720-570-2923

Response: See response to comment code 6120.

Commenter Name: L. Thorp
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0391
EPA Comment ID: 28465
EPA Comment Code: 6120

Comment: PLEASE KEEP ROCKET FUEL OUT OF OUR DRINKING WATER,I DON'T WANT TO IMBIBE A GLASS OF IT AND "TAKE OFF" THANK YOU FOR YOUR ATTENTION TO THIS MATTER

Response: See response to comment code 6120.

Commenter Name: R. Downing
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0396
EPA Comment ID: 28466
EPA Comment Code: 6120

Comment: The EPA should set a drinking water standard of no higher than 1 part per billion for perchlortae. This chemical does pose health risks and must be kept to a minimum.

Response: See response to comment code 6120.

Commenter Name: Sharon Biondi
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0401
EPA Comment ID: 28467
EPA Comment Code: 6120

Comment: Dear Sirs,

Please limit the chemical perchclorate in our water supplies to a safe level. The cumulative effect on our young and future generations is dangerous at the present level.

Thank you, Sharon Biondi

Response: See response to comment code 6120.

Commenter Name: Vorcelia Oliphant
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0410
EPA Comment ID: 28470
EPA Comment Code: 6120

Comment: Please do not permit these substances in our drinking water.

Thank you Vorcelia Oliphant

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0420
EPA Comment ID: 28472
EPA Comment Code: 6120

Comment: Please keep our water safe by eliminating use of perchlorate.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0435
EPA Comment ID: 28473
EPA Comment Code: 6120

Comment: Please no Perchlorate in our water supply. None.

Response: See response to comment code 6120.

Commenter Name: Andria Ventura
Commenter Organization: Clean Water Action et al.
EPA Document ID: EPA-HQ-OW-2009-0297-0528
EPA Comment ID: 28511
EPA Comment Code: 6120

Comment: From: Lenny Siegel To: Eric Burneson/DC/USEPA/US@EPA Cc: Andria Ventura Date: 09/18/2009 01:29 AM Subject: Re: Docket ID No. EPA-HQ-OW-2009-0297

Eric,

Please find attached a letter from community activists across the country calling upon EPA to regulate perchlorate and set a standard protective of ALL Americans.

Lenny Siegel

--

Lenny Siegel Executive Director, Center for Public Environmental Oversight a project of the Pacific Studies Center 278-A Hope St., Mountain View, CA 94041 Voice: 650/961-8918 or 650/969-1545 Fax: 650/961-8918

http://www.cpeo.org

Attachment

September 4, 2009

Mr. Eric Burneson Office of Ground Water and Drinking Water Standards and Risks Management Division Environmental Protection Agency 1200 Pennsylvania Avenue, NW, Mailcode 2822T Washington, D.C. 20460

Re: Docket ID No. EPA-HQ-OW-2009-0297

Dear Mr. Burneson,

On behalf of our various organizations and our tens of thousands of members throughout the United States, we are writing to express our belief that the potential health impacts from exposure to perchlorate through drinking water are significant and that they warrant prompt regulation to protect public health and safety. Setting a drinking water standard will provide the U.S. Environmental Protection Agency (EPA) with a "meaningful opportunity for health risk reduction for persons served by public water systems." Consequently, EPA should move as quickly as possible to establish a more protective reference dose for perchlorate and then to promulgate a maximum contaminant level (MCL) for perchlorate that is no higher than one part per billion (ppb). We base this view on the scope of the contamination in drinking water supplies, exposure of the American population through other pathways, including food, and the most recent scientific studies that demonstrate serious health threats, even at low levels, to a larger portion of the population than previously recognized. These studies are based upon a much larger exposure data set than the studies upon which the current reference dose, and thus the entire regulatory regime, is based.

Response: Regarding "establishing a more protective reference dose for perchlorate," see response to comment code 2110. Regarding EPA's decision to regulate perchlorate, see response to comment code 6120.

Commenter Name: Andria Ventura
Commenter Organization: Clean Water Action et al.

EPA Document ID: EPA-HQ-OW-2009-0297-0528
EPA Comment ID: 28517
EPA Comment Code: 6120

Comment: A perchlorate drinking water standard of no higher than 1 ppb would protect a large share of the American population currently at risk. Given the scope of the perchlorate contamination nationally, the multiple exposure pathways and other environmental contaminants impacting thyroid function and development, and the data demonstrating a serious health threat to a significant part of the country's population, EPA is obligated to establish such a drinking water standard. We applaud the agency's consideration of how to move forward to regulate this contaminant and urge you to take steps to establish a protective MCL as soon as possible.

Sincerely,

Andria Ventura Program Manager Clean Water Action San Francisco, CA

Lenny Siegel Executive Director Center for Public Environmental Oversight Mountain View, CA

Jeanne Rizzo, R.N. President Breast Cancer Fund San Francisco, CA

Debra Hall Founder Hopewell Junction Citizens for Clean Water Hopewell Junction, NY

Peter Strauss President PM Strauss & Associates San Francisco, CA

Pamela King Palitz Environmental Health Advocate and Staff Attorney Environment California San Francisco, CA

Ansje Miller Policy Director Center for Environmental Health Oakland, CA

Jerry Bowling III Behr VOC Area Leaders Dayton, Ohio

Brian Moench, MD President Utah Physicians for a Healthy Environment

David W. Campbell Secretary-Treasurer USW Local 675 Carson, CA

Steven B. Pollack, Attorney Executive Director Blue Eco Legal Council Northbrook, IL

Stephen M. Brittle Don't Waste Arizona Phoenix, AZ

Dvija Michael Bertish Rosemere Neighborhood Association Vancouver, WA

Luis Olmedo Velez Executive Director Comite Civico del Valle, Inc. Brawley, CA

Kent Slowinski Environmental Health Group Washington, D.C.

Laura Olah, Executive Director Citizens for Safe Water Around Badger Merrimac, WI

Miriam Torres Environmental Justice Coalition for Water Santa Monica, CA

Chris Nidel, M.S., J.D. Nidel Law, PLLC

Jane Horton Mountain View, CA

Dave Ness, Jr Bayport, MN

John Yelenick SSAB - Rocky Mountain Arsenal Denver, CO

Stephanie Smolen Former resident San Gabriel Valley, CA

Barry Kissin, Esq. Member Fort Detrick Restoration Advisory Board Frederick, MD

Gail Shephard Norwalk, CA

Bruce Oldfield Professor, Geology Broome Community College Binghamton NY

Bob Spiegel Executive Director Edison Wetlands Association Edison, NJ

Robert Stewart Rural Community Assistance Project Washington DC

Response: See response to comment code 6120.

Commenter Name: Kathy Curtis
Commenter Organization: Alliance of Nurses for Healthy Environments (ANHE)
EPA Document ID: EPA-HQ-OW-2009-0297-0651
EPA Comment ID: 28541
EPA Comment Code: 6120

Comment: October 7, 2009

Mr. Eric Burneson Office of Ground Water and Drinking Water Standards and Risks Management Division Environmental Protection Agency 1200 Pennsylvania Avenue, NW, Mailcode 2822T Washington, D.C. 20460 Re: Docket ID No. EPA-HQ-OW-2009-0297

Dear Mr. Burneson,

On behalf of The Alliance of Nurses for Healthy Environments, we are writing to express our belief that the potential health impacts from exposure to perchlorate through drinking water are significant and that they call for prompt regulation to protect the public's health and safety. Setting a drinking water standard will provide the U.S. Environmental Protection Agency (EPA) with a "meaningful opportunity for health risk reduction for persons served by public water systems". EPA should move as quickly as possible to establish a more protective reference dose for perchlorate and then to promulgate a maximum contaminant level (MCL) for perchlorate that is no higher than one part per billion (ppb).

Response: See response to comment code 6120.

Commenter Name: Kathy Curtis
Commenter Organization: Alliance of Nurses for Healthy Environments (ANHE)
EPA Document ID: EPA-HQ-OW-2009-0297-0651
EPA Comment ID: 28546
EPA Comment Code: 6120

Comment: A perchlorate drinking water standard of no higher than 1 ppb would protect a large share of the American population currently at risk. Given the scope of the perchlorate contamination nationally, the multiple exposure pathways and other environmental contaminants impacting thyroid function and development, and the data demonstrating a serious health threat to a significant part of the country's population, we believe EPA is obligated to establish such a drinking water standard. We applaud the agency's consideration of how to move forward to regulate this contaminant and urge you to take steps to establish a protective MCL as soon as possible.

We look forward to following the EPA response on this critical health issue.

Sincerely, Kathy Curtis and MaryJane Williams, RN, PhD Co-chairs, Policy Workgroup For the Alliance of Nurses for Healthy Environments

Response: See response to comment code 6120.

Commenter Name: Rebecca O'Donnell
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0436
EPA Comment ID: 28581
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion perchlorate, if that!

Sincerely, Rebecca O'Donnell Boyertown, PA

Response: See response to comment code 6120.

Commenter Name: Raymond Sowiak
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0440
EPA Comment ID: 28582
EPA Comment Code: 6120

Comment: I urge the EPA to adopt a limit of 1 PPBW perchlorate in U.S. drinking water. I understand recent studies show perchlorate to be more harmful than previously thought, especially to infants and young children. It may cause mental retardation, loss of hearing and speech, and poor development of motor skills.

EPA's own data show perchlorate to be present in drinking water in 37 states, including public water systems serving more than 20 million people.

I understand that perchlorate, like any harmful chemical, probably affects different people to different degrees, but I also believe the EPA should err on the conservative side until more data can be amassed regarding the effects of these chemicals on a decent statistical basis. Big business will always have powerful advocates and lobbyists presenting gloomy scenarios of high costs and dubious benefits, but who advocates for the average guy here in the U.S.?

Response: See response to comment code 6120.

Commenter Name: Ron Harden
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0441
EPA Comment ID: 28583
EPA Comment Code: 6120

Comment: It is imperative that our drinking water be protected in every possible way. It us unconsciensionable that perchlorate would be allowed to enter it, and unconsciensionable of an industry to seek to be able to place the compound in ground water. Please issue the appropriate regulation to disallow perchlorate from being placed into our water supplies.

Response: Perchlorate is not being placed into water systems. EPA has decided to regulate perchlorate. See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0445
EPA Comment ID: 28584
EPA Comment Code: 6120

Comment: Let's go! Complete this drinking water standard.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0446
EPA Comment ID: 28585
EPA Comment Code: 6120

Comment: Please set limits for perchlorate in drinking water. It surprises me that it would even be considered not to have regulated and enforced standards to protect our citizens.

Thank you!

Response: See response to comment code 6120.

Commenter Name: Eva
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0453

EPA Comment ID: 28586
EPA Comment Code: 6120

Comment: Dear Trusted employees at Environmental Protection Agency of the USA,

The citizens of this country trust you to analyze every single substance that comes at all in contact with our living environment, and to determine what amounts we can tolerate and still be healthy. We, including industry, needs to know that, so we can act accordingly.In your spare time you need to do that. But since you don't have any spare time ... then prioritize! and do the ones that are obvious first!

Perchlorate is one of the very obvious ones that need to be done now! And please remember, that if you wait till a chemical is at the top of the priority list, then your analysis is more likely to be tainted by politics or industry pressures. It's better to get it done early, while no one is paying attention, so you can make a true impact analysis .... and please, always err on the side of human safety .... better to be safe than sorry. Thanks kindly ... we're counting on you to protect us. Eva in Denver, CO

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0466
EPA Comment ID: 28589
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a primary drinking water standard for perchlorate that prioritizes potential and proven risks to public health and ecosystems over risks to industries that use perchlorate.

Perchlorate is a harmful chemical that EPA claims has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher. Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism. Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

Response: See response to comment code 6120.

Commenter Name: Daniel Sullivan
Commenter Organization: Foil The Three Productions
EPA Document ID: EPA-HQ-OW-2009-0297-0474
EPA Comment ID: 28590
EPA Comment Code: 6120

Comment: Keep this perchlorate, this ingredient of rocket fuel, out of people's drinking water. Everyone has a right to be uncontaminated, especially children, who need to develop well. This stuff can retard their ability to build a good life in this changing world.

Response: See response to comment code 6120.

Commenter Name: Donna Cirillo
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0475
EPA Comment ID: 28591
EPA Comment Code: 6120

Comment: To Whom It May Concern,

I don't understand what the debate is about. We know that Perchlorate affects the thyroid, so limit it's usage. How many people need to be harmed before you take action?

Very concerned citizen. Donna Cirillo

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0476
EPA Comment ID: 28592
EPA Comment Code: 6120

Comment: Please take action to limit perchlorate in drinking water.

Nobody wants rocket fuel in their drinking water. However, the U.S. Environmental Protection Agency (EPA) has still not decided whether to set a drinking water standard - a limit - for perchlorate, an ingredient in rocket fuel that is contaminating water nationwide.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0479
EPA Comment ID: 28593
EPA Comment Code: 6120

Comment: Please Regulate our water more effectively and efficiently.

Response: See response to comment code 6120.

Commenter Name: Cici Hallberg
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0481
EPA Comment ID: 28594
EPA Comment Code: 6120

Comment: Please keep perchlorate out of our drinking water. It has been determined to be carcinogenic. We don't need any more contaminates in our drinking water.

Response: See response to comment code 6120.

Commenter Name: Belina Reisman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0483
EPA Comment ID: 28595
EPA Comment Code: 6120

Comment: Please protect us from another pollutant. Please set limits on percholate in our water.

Just today, I've come across two items that highlight our need to keep water safe and available, which requires regulatiion.

The first, a news article, addressed peoples' need for dental work due to the damaging pollutants in the water.

The second was a documentary shown on TV - Flow: For the Love of Water. I came away from the show recognizing we need to work now for protection of our water resources.

Then, Clean Water Action sent me an email on the percholate issue.

Response: See response to comment code 6120.

Commenter Name: Lynn surname not provided
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0487
EPA Comment ID: 28596
EPA Comment Code: 6120

Comment: Please make sure that percholate does not get into our water.It affects everyone. Keep us safe.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0488
EPA Comment ID: 28597
EPA Comment Code: 6120

Comment: Please remain true to your name: the Environmental Protection Agency. That means something. This is not a conditional protection you offer, as in when you get special interest money to loosen controls, etc. You are charged with protecting the environment UNCONDITIONALLY. Please do your job. Keep our drinking water clean. Keep perchlorate out.

Response: See response to comment code 6120.

Commenter Name: Keitha Kinne
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0489
EPA Comment ID: 28598
EPA Comment Code: 6120

Comment: I strongly urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate. For too long we have put the interest of unbridled growth ahead of the health of our people and our environment. We must recognize that we cannot continue down this path and the EPA must become a strong voice for preserving our environment.

It is evident that perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; protecting infants and children is critical. A national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Please take this important step to limit perchlorate contamination. Respectfully yours. Keitha Kinne, 129 Picketts Ridge Road, Redding CT 06896

Response: See response to comment code 6120.

Commenter Name: William Connor
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0490
EPA Comment ID: 28599
EPA Comment Code: 6120

Comment: Please prohibit perchlorate out of potable water. Thank you

Response: See response to comment code 6120.

Commenter Name: Sasha Rickard
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0503
EPA Comment ID: 28601
EPA Comment Code: 6120

Comment: Dear EPA,

I am strongly in favor of puting a standard of no more than 1 part per billion for perchlorate as it is a risk to public health.

Sincerely, Sasha Rickard

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:

EPA Document ID: EPA-HQ-OW-2009-0297-0508
EPA Comment ID: 28602
EPA Comment Code: 6120

Comment: I ask you, please, U.S. Environmental Protection Agency, to put a limit on the amount of perchlorate in our drinking water to no higher than 1 part per billion.

The public, of all ages, deserves to have their health protected by drinking water that does not cause health problems. If we as citizens do not have our health, we do not have much at all.

Response: See response to comment code 6120.

Commenter Name: Barbara Mc Ellen
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0512
EPA Comment ID: 28603
EPA Comment Code: 6120

Comment: iam a single voter in bergen county new jersey who is recovering from cancer. please get the pollutants out of our water..including rocket fuel!!!!

Response: See response to comment code 6120.

Commenter Name: Ryan Tomazin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0520
EPA Comment ID: 28605
EPA Comment Code: 6120

Comment: I am an environmental protection science/chemistry graduate, and I constantly argued with professors, guests from ALCOSAN in Pittsburgh and everyone else that would listen about chemical levels in water and what was acceptable in drinking water. Water is essential to all life, and there should not be an acceptable level of rocket fuel in water. There should be NO rocket fuel, or PCBs or heavy metals, etc., in our water. The water authorities should not have to super- chlorinate our water, like it is in Pittsburgh, to give us something that is essential to our life. Stand up and be the Environmental Protection Agency, and not the Chemical Subsidiaries Protection Agency. You were supposed to be on our side. How many cancer deaths do we have in the US, compared to 30 or 50 years ago? Clean air and water is necessary, not optional. We are paying you, and this is what we want.

Thank you for your time,

Ryan Tomazin Bridgeville, PA

Response: See response to comment code 6120.

Commenter Name: Alexandra Grabbe
Commenter Organization: Chez Sven Bed & Breakfast

EPA Document ID: EPA-HQ-OW-2009-0297-0524
EPA Comment ID: 28606
EPA Comment Code: 6120

Comment: I run a green bed & breakfast in Wellfleet on Cape Cod and often comment about the state of water on our fragile sandbar. I am very worried about percholorate in water supplies, since I have traveled on airplanes that dumped rocket fuel into the ocean, and sincerely hope you will do something to control percholorate. Please set a standard and improve regulations regarding drinking water in general. Thank you for your attention.

Response: See response to comment code 6120.

Commenter Name: Kathy Dolan
Commenter Organization: Food and Water Watch (FWW)
EPA Document ID: EPA-HQ-OW-2009-0297-0526
EPA Comment ID: 28607
EPA Comment Code: 6120

Comment: Dear Administrator Jackson,

Attached you will find an official statement from Food and Water Watch regarding EPA-HQ-OW-2009-0297. Additionally, we have included over 6,000 activist letters supporting our statement.

We urge you to make a national primary drinking water rule for perchlorate. EPA's failure to regulate perchlorate in drinking water places consumers, especially children and pregnant women, at risk. We recommend that EPA use the regulation of perchlorate as an opportunity to protect our waterways and make our drinking water safe for all.

Thank you for your consideration,

Kathy Dolan Triclosan Campaign Advocate Food and Water Watch

Attachment

Administrator Jackson USEPA Headquarters Ariel Rios Building 1200 Pennsylvania Avenue, N. W. Washington, DC 20460

September 18, 2009

Dear Administrator Jackson,

I am writing, on behalf of Food and Water Watch, to urge you to make a national primary drinking water rule for perchlorate.

Response: See response to comment code 6120.

Commenter Name: Kathy Dolan
Commenter Organization: Food and Water Watch (FWW)

EPA Document ID: EPA-HQ-OW-2009-0297-0526
EPA Comment ID: 28612
EPA Comment Code: 6120

Comment: The widespread exposure of the population to some level of perchlorate raises serious health concerns. Perchlorate can inhibit the thyroid glands iodine uptake, potentially leading to hypothyroidism. Severe hypothyroidism during pregnancy can lead to abnormal fetal cognitive development, and even mild hypothyroidism during pregnancy is associated with subtle cognitive defects in children. Thus, perchlorate could alter fetal brain development, having lifelong cognitive effects for those affected.

EPA's failure to regulate perchlorate in drinking water places consumers, especially children and pregnant women, at risk. We urge the EPA to consider the regulation of perchlorate as an opportunity to protect our waterways and make our drinking water safe for all.

Sincerely,

Kathleen Dolan Triclosan Campaign Advocate

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0535
EPA Comment ID: 28613
EPA Comment Code: 6120

Comment: I have lived on the "space coast" for over 40 years. I have an immune illness and wonder how much all those launches and resulting rocket fuel in my air and water may have contributed to my chronic illness. I will never have good health again. I don't want others to go through this miserable life. We must clean our air and water and this includes getting perchlorate out of our environment.

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #11 - Food and Water Watch
EPA Document ID: EPA-HQ-OW-2009-0297-0526
EPA Comment ID: 28614
EPA Comment Code: 6120

Comment: Administrator Jackson USEPA Headquarters Ariel Rios Building 1200 Pennsylvania Avenue, N. W. Washington, DC 20460

September 18, 2009

Dear Administrator Jackson,

I am writing, on behalf of Food and Water Watch, to urge you to make a national primary drinking water rule for perchlorate.

Perchlorate has been found in the drinking water supply of 35 states and the District of Columbia. Widespread human exposure to perchlorate was confirmed by the Center for Disease Control's NHANES study, which found that 100 percent of the 2,820 randomly selected study participants had detectable levels of perchlorate in their urine. And according to your request for comment notice, dated August 5, 2009, the number of people served by water contaminated with high levels of perchlorate ranges between 53.4 and 16.8 million people.

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #11 - Food and Water Watch
EPA Document ID: EPA-HQ-OW-2009-0297-0526
EPA Comment ID: 28618
EPA Comment Code: 6120

Comment: The widespread exposure of the population to some level of perchlorate raises serious health concerns. Perchlorate can inhibit the thyroid glands iodine uptake, potentially leading to hypothyroidism. Severe hypothyroidism during pregnancy can lead to abnormal fetal cognitive development, and even mild hypothyroidism during pregnancy is associated with subtle cognitive defects in children. Thus, perchlorate could alter fetal brain development, having lifelong cognitive effects for those affected.

EPA's failure to regulate perchlorate in drinking water places consumers, especially children and pregnant women, at risk. We urge the EPA to consider the regulation of perchlorate as an opportunity to protect our waterways and make our drinking water safe for all.

Response: See response to comment code 6120.

Commenter Name: Mic Stewart
Commenter Organization: Water Quality Section, Metropolitan Water District of Southern California
EPA Document ID: EPA-HQ-OW-2009-0297-0496
EPA Comment ID: 28710
EPA Comment Code: 6120

Comment: Metropolitan's Concerns

Perchlorate contamination entering the Colorado River from the Las Vegas Wash area represents the largest extent of perchlorate contamination in the country. Water from the Colorado River downstream of the Las Vegas Wash supplies drinking water for over 23 million people throughout Nevada, California, and Arizona. Any effort to regulate perchlorate would ensure some degree of public health protection for this source of water supply. Metropolitan believes that federal regulation of perchlorate would provide a meaningful opportunity for health risk reduction for the public water systems as described in the Safe Drinking Water Act.

Response: See response to comment code 6120.

Commenter Name: Mic Stewart
Commenter Organization: Water Quality Section, Metropolitan Water District of Southern California
EPA Document ID: EPA-HQ-OW-2009-0297-0496
EPA Comment ID: 28714
EPA Comment Code: 6120

Comment: Since the 1996 amendments to the Safe Drinking Water Act, no new contaminant has met EPA's three criteria for national primary drinking water regulation. Metropolitan believes that a determination by EPA not to regulate perchlorate in drinking water could adversely influence cleanup efforts along the Colorado River and other contaminated sites.

Metropolitan appreciates this opportunity to provide comments on scientific approaches to analyzing scientific data related to perchlorate in drinking water and requests that EPA carefully consider these comments. Please contact me at (213) 217-5696 if you have any questions, or if I can provide additional information.

Very truly yours, Mic Stewart, Ph. D. Manager, Water Quality Section

Response: See response to comment code 6120.

Commenter Name: Nsedu O. Witherspoon
Commenter Organization: Children's Environmental Health Network
EPA Document ID: EPA-HQ-OW-2009-0297-0674
EPA Comment ID: 28737
EPA Comment Code: 6120

Comment: The Network believes that the potential health impacts from exposure to perchlorate through drinking water are significant and that they warrant prompt regulation to protect public health and safety. Setting a drinking water standard will provide the U.S. Environmental Protection Agency (EPA) with a "meaningful opportunity for health risk reduction for persons served by public water systems".

Consequently, EPA should move as quickly as possible to establish a more protective reference dose for perchlorate and then to promulgate a maximum contaminant level (MCL) for perchlorate that is no higher than one part per billion (ppb). We base this view on the scope of the contamination in drinking water supplies, exposure of the American population through other pathways, including food, and the most recent scientific studies that demonstrate serious health threats, even at low levels, to a larger portion of the population than previously recognized. These studies are based upon a much larger exposure data set than the studies upon which the current reference dose, and thus the entire regulatory regime, is based.

Perchlorate has been found in more than 400 drinking water sources in 26 states, potentially affecting tens of millions of people. EPA's own data say that nearly 17 million people receive their water from public water systems where perchlorate has been found at levels exceeding 4 ppb. Were sampling routinely conducted with a detection limit of 1 ppb, that number would be much higher-

particularly considering the estimated 20 million people in the Southwest who receive drinking water from the Colorado River.

Response: See response to comment code 6120.

Commenter Name: Nsedu O. Witherspoon
Commenter Organization: Children's Environmental Health Network
EPA Document ID: EPA-HQ-OW-2009-0297-0674
EPA Comment ID: 28742
EPA Comment Code: 6120

Comment: A perchlorate drinking water standard of no higher than 1 ppb would protect a large share of the American population currently at risk. Given the scope of the perchlorate contamination nationally, the multiple exposure pathways and other environmental contaminants impacting thyroid function and development, and the data demonstrating a serious health threat to a significant part of the country's population, EPA is obligated to establish such a drinking water standard. We applaud the agency's consideration of how to move forward to regulate this contaminant and urge you to take steps to establish a protective MCL as soon as possible.

Sincerely,

Nsedu O. Witherspoon, MPH Executive Director

Response: See response to comment code 6120.

Commenter Name: Dan Delventhal
Commenter Organization: MowGreen.US
EPA Document ID: EPA-HQ-OW-2009-0297-0270
EPA Comment ID: 28758
EPA Comment Code: 6120

Comment: Folks, we have to be proactive and precautionary and stand up as stewards to protect the masses from poisons in the air and water we survive on. You know the links to disease and reproductive related compromises. It would retarded to fail to prevent retardation in future generations. Limit Perchlorate!

Response: See response to comment code 6120.

Commenter Name: Karen Ceci
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0287
EPA Comment ID: 28759
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate. Please give our children and their children a chance at a healthy life.

Karen Ceci 11 Chalfont Rd Chalfont, PA 18914

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0536
EPA Comment ID: 28760
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate. Perchlorate contamination is a nationwide problem and has health impacts.

The US needs national primary drinking water regulations to protect public health not only from perchlorate but from chemicals used in hydraulic fracturing and other industrial practices currently unregulated as a result of the Bush administration. The EPA MUST take action NOW--what in the world are you waiting for? Surely in this administration the PEOPLE have rights to health?

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120. Regarding the need for drinking water regulations for contaminants used in hydraulic fracturing and other industrial practices, a response is not necessary because it is outside of the scope of this action.

Commenter Name: Rita Valent
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0547
EPA Comment ID: 28761
EPA Comment Code: 6120

Comment: I can't think of any reason why perchlorate shouldn't be limited. Of course it should be limited...it's dangerous, it hurts people. What other reason do we need?

Response: See response to comment code 6120.

Commenter Name: John M. Huff
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0549
EPA Comment ID: 28763
EPA Comment Code: 6120

Comment: I strongly request that the U.S. Environmental Protection Agency proceed with setting the drinking water standard for perchlorate at no higher than 1 part per billion, for the best interests of public health, particularly on behalf of infants and children. Thank you.

Response: See response to comment code 6120.

Commenter Name: Myrna Poticha

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0552
EPA Comment ID: 28764
EPA Comment Code: 6120

Comment: Please act vigorously to curtail the level of perchlorate in drinking water. Our drinking water supplies should be maintained at the highest level of purity, and exotic substances such as perchlorate have no place there, unless and until they are absolutely proven to be safe.Myrna Poticha Colorado

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0559
EPA Comment ID: 28766
EPA Comment Code: 6120

Comment: Rocket fuel: KEEP IT OUT OF OUR WATER SUPPLIES!!!

Response: See response to comment code 6120.

Commenter Name: Kevin Hammond
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0560
EPA Comment ID: 28767
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; protecting infants and children is critical.a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Although I am not sure if 1 ppb (part per billion) is a realistic level, the current level of air travel is only increasing warranting serious review of safe levels. We owe it to our children (and their's) to, at the very least, set a realistic regulatory level that is 1.) not cost-prohibitive, 2.) safe and 3.) maintainable.

Thank you for attention to this matter.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0563
EPA Comment ID: 28769

EPA Comment Code: 6120

Comment: Perchlorate, like all other man-made substances, should be filtered from all public water systems.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0567
EPA Comment ID: 28770
EPA Comment Code: 6120

Comment: eriously limit perchlorate in water, please. Thank you.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0574
EPA Comment ID: 28772
EPA Comment Code: 6120

Comment: please remove perchlorate from our drinking water keep our children safe from harm

Response: See response to comment code 6120.

Commenter Name: Carol Leventhal
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0583
EPA Comment ID: 28773
EPA Comment Code: 6120

Comment: It is inconceivable that the United States water supply is contaminated by perchlorate, to a degree that threatens health and well being. Please reduce perchlorate in the water to no more than 1 part per billion.

Carol Leventhal 9219 Manchester Road Silver Spring, MD. 20901

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0584
EPA Comment ID: 28774
EPA Comment Code: 6120

Comment: I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate. * perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; protecting infants and children is critical. * a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Recently, a defense analysis postulates that the world will be competing for water resources. in the light of this we cannot afford to further pollute our sources of fresh water with any more chemicals. Further we must hold the polluters responsible for any cleanup of known harmful chemicals in our water supplies.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0585
EPA Comment ID: 28775
EPA Comment Code: 6120

Comment: Perchlorate in drinking water is a public health problem.Even in small amounts, it can impair the thyroid gland, which controls growth, development and metabolism. Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

I urge the U.S. Environmental Protection Agency to establish and enforce a drinking water standard for perchlorate of no higher than 1 part per billion.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0591
EPA Comment ID: 28776
EPA Comment Code: 6120

Comment: Bearing in mind the mission the EPA should strive to fulfill: protecting our air, soil, and water.....I implore you to determine how the perchlorate is contaminating our water and to stop it.If stopping it is too lofty a goal for now, please limit the amount we are unknowingly exposed to every day. That's why we have your department - to protect citizens.

Response: See response to comment code 6120.

Commenter Name: Cathy Ellis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0597
EPA Comment ID: 28777
EPA Comment Code: 6120

Comment: I urge the Federal government to set a percolate standard of no more than 1 part per billion. Clean drinking water should be a right of every American. Contaminants hurt the smallest and weakest the most and can be very harmful to fetuses and infants. These helpless citizens need the government to protect them over before it protects the rights of corporate America. Cathy Ellis West Chazy, NY

Response: See response to comment code 6120.

Commenter Name: Jim Tate
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0607
EPA Comment ID: 28779
EPA Comment Code: 6120

Comment: EPA: Please establish a standard for the volume of perchlorate permitted in our drinking water. And it should be extrememly low! Enough scientific data exist to convince EPA that perchlorate is hazardous to the health of anyone living in the US.

Response: See response to comment code 6120.

Commenter Name: Neeka Stanley
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0611
EPA Comment ID: 28781
EPA Comment Code: 6120

Comment: I drink tap water and I don't want a dose of perchlorate with it! It's a ridiculous waste to buy bottled water- I need my tap water to be safe and clean. I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate. I work with kids with special needs and see the constant strain it puts on the kids, their families, and our community as we care for these kids. We need to do everything we can to limit exposure to toxic chemicals that could lead to even more kids with special needs. Thank you.

Response: See response to comment code 6120.

Commenter Name: Joanne R. Hand
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0613
EPA Comment ID: 28782
EPA Comment Code: 6120

Comment: As a concerned citizen and supporter of Clean Water action I want to express my concern that the EPA limit the levels of perchlorate in drinking water to a standard of no higher than 1 part per billion for perchlorate

Joanne R. Hand 41 Gregory Terrace Bloomfield New Jersey 07003

Response: See response to comment code 6120.

Commenter Name: James Griffin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0618
EPA Comment ID: 28783
EPA Comment Code: 6120

Comment: I am writing to condemn the idea of allowing perchlorate in drinking water. In considering standards for water purity I urge you disallow this carcinogen in our water.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0619
EPA Comment ID: 28784
EPA Comment Code: 6120

Comment: However, the U.S. Environmental Protection Agency (EPA) has still not decided whether to set a drinking water standard - a limit - for perchlorate, an ingredient in rocket fuel that is contaminating water nationwide.

Clean Water Action members can help make sure the EPA takes action to limit perchlorate in drinking water.

On August 19, the U.S. Environmental Protection Agency (EPA) requested public comments related to setting a limit for perchlorate in drinking water. Last year EPA appeared poised to announce that it would not set a limit but is now reviewing scientific and other information to make a decision about moving forward with a regulation now.

Why limit perchlorate?

Perchlorate is a harmful chemical that EPA claims has been found in 395 sites in 37 states, including 153 public water systems serving over 20 million people. Some estimates are even higher.

Perchlorate, even in small amounts, can impair the thyroid gland, which controls growth, development and metabolism.

Developing fetuses, infants and children with thyroid impairment may suffer mental retardation, loss of hearing and speech or deficits in motor skills.

Sample Letter

I urge the U.S. Environmental Protection Agency to move forward with a drinking water standard of no higher than 1 part per billion for perchlorate.

perchlorate contamination is a nationwide problem and has health impacts at lower levels than previously thought; protecting infants and children is critical.a national primary drinking water regulation would provide a meaningful opportunity to protect public health.

Response: This is not a comment, a response is not needed.

Commenter Name: Lucy Rogers
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0621
EPA Comment ID: 28785
EPA Comment Code: 6120

Comment: Keep perchlorate out of our drinking water.

Response: See response to comment code 6120.

Commenter Name: Barbara B. Tacy
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0623
EPA Comment ID: 28786
EPA Comment Code: 6120

Comment: To Whom It May Concern; As an individual living in a highly populated area I am very aware of the critical need to protect what clean water we have left. Please act now to restrict the introduction of perchlorate into all of our water systems. Thank you, Dr. Barbara B. Tacy

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0624
EPA Comment ID: 28787
EPA Comment Code: 6120

Comment: make this happen, we should not have to drink this

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0629
EPA Comment ID: 28788
EPA Comment Code: 6120

Comment: I don't understand how it is acceptable for any perchlorate to be in any water in America. I do not feel that the government has the people's best interest in mind when they allow these chemicals into homes. During the presidential campaign, I noticed there was a lot of talk about preventative care for health. I feel this goes in with that. If we were to take care of the roots of

sickness and disease, then the tree would die off as well. The government has a responsibility to the people of America, and I feel that it is about time that the government steps up and fulfills those responsibilities.

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0630
EPA Comment ID: 28789
EPA Comment Code: 6120

Comment: I don't understand how it is acceptable for any amount of perchlorate to be in any water in America. During the presidential campaign, there was a lot of talk about preventative care. If we prevented the public from consuming harmful chemical, we would also be preventing the public from becoming ill. The government has a responsibility to the American people. I think it is about time the government steps up and fulfills those responsibilities.

Response: See response to comment code 6120.

Commenter Name: Brad Heinz
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0631
EPA Comment ID: 28790
EPA Comment Code: 6120

Comment: From 1962-1977, I was raised in West Covina, California, a city whose drinking water supply was later determined to be contaiminiated by perchlorate. In late 1977, after I left for college, I was diagnosed with thyroid disease. The disease made it very difficult to pursue my studies, forcing me to drop classes. It also significantly intefered with my social integration during my freshman year. When later I learned about the contamination of the water supply in West Covina, I was angry to think how that might have contributed to the disease. It wrecked my life for the period leading up to diagnosis and treatment. I'm still concerned about the longterm health effects. Please strictly regulate this chemical in our drinking water.

Response: See response to comment code 6120.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28792
EPA Comment Code: 6120

Comment: September 19, 2009

U.S. Environmental Protection Agency Office of Water Docket (Mailcode: 2822T) 1200 Pennsylvania Avenue, NW Washington, DC 20460

Submitted via www.regulations.gov

Comments from the NATURAL RESOURCES DEFENSE COUNCIL

on the Drinking Water: Perchlorate Supplemental Request for Comments

Docket EPA-HQ-OW-2009-0297 Federal Register / Vol. 74, No. 159/ Wednesday, August 19, 2009

SUMMARY

On August 19, 2009, the U.S. Environmental Protection Agency (EPA) issued a Federal Register (FR) notice[FN1: 74 Fed. Reg. 41883 (August 19, 2009).] requesting comments on additional approaches to analyzing data related to its perchlorate preliminary determination as detailed in its October 10, 2008 FR Notice.[FN2: 73 Fed. Reg. 60262 (October 10, 2008).] In that previous notice, EPA made a preliminary regulatory determination not to set a health-protective standard for perchlorate in drinking water.[FN3: Id.] It stated, "The Agency has determined that a national primary drinking water regulation (NPDWR) for perchlorate would not present 'a meaningful opportunity for health risk reduction for persons served by public water systems.'" EPA also proposed a health reference level (HRL) of 15 parts per billion (ppb) as the maximum contamination level of perchlorate that could be in drinking water and still keep daily human consumption levels from exceeding the reference dose (RfD) of 0.7 ug/kg/day.

In response to the October 10, 2008 FR notice, NRDC provided comments to EPA concluding that EPA's determination was legally flawed. EPA must regulate a contaminant if it may have an adverse effect on human health, if it is known to occur (or there is a substantial likelihood that the contaminant will occur) in public water systems with a frequency and at levels of public health concern; and if its regulation would present a meaningful opportunity for health risk reduction for persons served by public water systems.[FN4: 42 U.S.C. [Sec] 300g-1(b)(1)(A).] For perchlorate, each of these three requirements are met, and therefore, underscore the need for EPA to regulate its presence in drinking water. First, EPA's preliminary regulatory determination acknowledges that perchlorate may adversely affect human health.[FN5: 73 Fed. Reg. 60275 (Oct. 10, 2008).] Second, as explained in more detail below, despite EPA's contention, perchlorate is known to contaminate the drinking water systems serving millions of people at levels where adverse human health effects occur. And third, setting an appropriately stringent MCL will lead to lower levels of perchlorate ingested by hundreds of thousands of infants, children, and pregnant women, thereby offering a concrete and meaningful reduction in human health risks.

The U.S. population is about 300 million people with about 6.8%, or 20 million, under 5 years old. Therefore, based on EPA estimates that 16.6 million people are served by public water system with at least one detection of perchlorate over 4 ppb, there are, therefore, likely more than one million children in each year of life (from zero to five) who may be exposed to perchlorate levels that may adversely affect their health.[FN6: This value is derived by multiplying 16.6 million by 0.068. Please see below for further explanation about the appropriate perchlorate level to set for the health reference level.] Thus, the evidentiary record does not support EPA's proposed determination. Rather, the evidentiary record makes clear that regulating these exposures do represent "a meaningful opportunity for health risk reduction for persons served by public water systems."

Based upon the evidence in the record, as discussed in greater detail below, NRDC urges EPA to reverse course, and set a national primary drinking water standard for perchlorate that is protective of sensitive sub-populations. EPA should not set a HRL at 15 ppb; rather, given the most current data available, NRDC believes that to truly protect the public health, EPA should set an enforceable maximum contaminant level (MCL) as authorized by the Safe Drinking Water Act below 1 ppb.

Response: See response to comment code 6120.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28796
EPA Comment Code: 6120

Comment: NRDC strongly objected to EPA's preliminary determination not to regulate perchlorate because the conclusions are not based on a comprehensive review of the best available science (as explained in more detail below) and are not supported by the PBPK model findings, or by EPA's expert scientific advisors on the Children's Health Protection Advisory Committee.[FN23: Letter from Melanie Marty to Administrator Johnson regarding Preliminary Regulatory Determination on Perchlorate (November 3, 2008, PDF) http://yosemite.epa.gov/ochp/ochpweb.nsf/content/perchlorateletter.htm/$file/PerchlorateLetter.pdf] In fact, drinking water that is contaminated with perchlorate at the proposed HRL of 15 ppb would leave infants and young children exposed to excessive and unsafe levels of this toxic chemical.

Response: See response to comment ID 20988 under comment code 6120.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28812
EPA Comment Code: 6120

Comment: ADDITIONAL COMMENTS

Regulating Perchlorate Represents a Meaningful Opportunity for Health Risk Reduction

NRDC notes that there is enough information for the Agency to make a final regulatory determination to promulgate a national primary drinking water standard for perchlorate. The evidence about the impact of perchlorate contaminated drinking water shows that it satisfies the requirements for promulgating a drinking water standard under the Safe Drinking Water Act: (1) perchlorate is know to have an adverse effect on the health of persons; (2) perchlorate is known to occur in public water systems with a frequency and at levels of public health concern, and (3) regulating perchlorate presents a meaningful opportunity for health risk reduction for persons served by public water systems. Therefore, EPA should set an MCL for perchlorate, rather than focus on setting an HRL.

In its October 10, 2008 preliminary determination not to regulate perchlorate, EPA acknowledged that perchlorate could have an adverse effect on human health.[FN65: 73 Fed. Ref. at 60275.] Second, based on just quarterly or semi- annual sampling along, EPA showed that 4 percent of drinking water systems have detections of perchlorate over 4 ppb. As explained in further detail below, this occurrence exposes hundreds of thousands of pregnant women, children, and infants to dangerous levels of perchlorate, giving rise to a public health concern.

In October, 2008, EPA determined that up to 28,000 pregnant women would be exposed to more than 15 ppb of perchlorate. However, at that time, EPA stated that reducing the risk that 28,000 pregnant women would be exposed to perchlorate would not provide a meaningful opportunity to reduce health risks.

What that October 2008 announcement failed to explain is that EPA's own staff experts have provided data to show that at the proposed HRL of 15 ppb, infants and children would consume perchlorate on a daily basis that exceeded the reference dose.

As explained above, EPA's proposed model shows that there are over one million children under 5 years old who would exceed the daily reference dose; this is likely an underestimate of the highly exposed.

As noted above, NRDC believes that any amount of perchlorate in drinking water over 1 ppb may have adverse health impacts on vulnerable populations, meaning EPA's estimate of the number of pregnant women who would be exposed to excessive perchlorate would be much higher than 28,000. In fact, based on EPA's estimate, over 200,000 pregnant women could be exposed to perchlorate contamination over 4 ppb (the maximum detection limit identified in EPA's estimates). As such, by any measure, a regulation that could protect up to over 200,000 pregnant women and a million children and infants would give rise to a meaningful opportunity to protect public health.

Response: See response to comment code 6120.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28816
EPA Comment Code: 6120

Comment: CONCLUSION

EPA should amend its preliminary determination on perchlorate. EPA should determine to promulgate a national primary drinking water standard for perchlorate, to protect public health. Existing data on perchlorate exposure and effects, especially on vulnerable subpopulations, demonstrates that setting a national primary drinking water standard for perchlorate would provide a meaningful opportunity for health risk reduction. EPA is therefore required to set such a standard under the Safe Drinking Water Act.

Furthermore, a maximum contaminant level below 1 ppb would afford reasonable protections to the health of the susceptible populations of pregnant women and breast-fed infants.

Response: See response to comment code 6120.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Department of Environmental Protection (NJDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0527
EPA Comment ID: 28908
EPA Comment Code: 6120

Comment: NJ Environmental Protection's comment.

If problem looking, please call 609-292-5550, Heather Hansberry

Attachment

September 18, 2009

Water Docket Environmental Protection Agency Mail Code: 2822T 1200 Pennsylvania Ave, NW Washington, DC 20460 RE: Docket ID No. EPA-HQ-OW-2009-0297

To Whom It May Concern:

Thank you for the opportunity to provide comments on USEPA's notice, "Drinking Water: Perchlorate Supplemental Request for Comments," which was published in the Federal Register of August 18, 2009 (74 Fed. Reg. 41883-41893). On March 16, 2009, the New Jersey Department of Environmental Protection (NJDEP) proposed a drinking water Maximum Contaminant Level (MCL) of 5 ug/L, including monitoring and compliance determination requirements, in accordance with the 2005 recommendation of the New Jersey Drinking Water Quality Institute (NJDWQI), a legislatively created advisory body. The NJDEP believes that having an MCL for perchlorate will be beneficial to public health both in New Jersey and in the country as a whole.

In comments submitted on November 10, 2008, we urged USEPA to reconsider its October 10, 2008 proposed determination to not regulate perchlorate in drinking water. Our comments stressed that USEPA's proposed Health Reference Level (HRL) of 15 ug/L is not protective of infants, who are a sensitive population for perchlorate's effects on thyroid function. We also commented that the occurrence analysis presented was flawed because its use of an inappropriately high concentration, 15 ug/L, greatly reduced the size of the population predicted to be exposed at levels of public health concern. We commend USEPA for its current decision to reconsider its proposal not to regulate perchlorate, based on the comments submitted by us and by many others.

Response: This is not a comment, a response is not necessary.

Commenter Name: Jeanne Herb
Commenter Organization: New Jersey Department of Environmental Protection (NJDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0527
EPA Comment ID: 28917
EPA Comment Code: 6120

Comment: We also strongly urge USEPA to reconsider its determination to not regulate perchlorate. The NJDEP (2009) proposed rule regarding the regulation of perchlorate in drinking water can be found at http://www.nj.gov/dep/rules/proposals/031609a.pdf. The New Jersey Drinking Water Quality Institute (2005) recommendations regarding perchlorate can be found at http://www.nj.gov/dep/watersupply/perchlorate_mcl_10_7_05.pdf. For further information or clarification about this issue, please contact Dr. Gloria Post at (609) 292-8497 or gloria.post@dep.state.nj.us.

Sincerely, Jeanne Herb Director Policy, Planning and Science

Scott Brubaker Acting Assistant Commissioner Land Use Management

C : Gary Buchanan, NJDEP Judy Louis, NJDEP Sandra Krietzman, NJDEP Betty Boros-Russo, NJDEP Gloria Post, NJDEP Perry Cohn, NJDHHS Mark Robson, Chair, New Jersey Drinking Water Quality Institute

Response: See response to comment code 6120.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group (EWG)
EPA Document ID: EPA-HQ-OW-2009-0297-0499
EPA Comment ID: 28926
EPA Comment Code: 6120

Comment: Attached are EWG's comments on Docket ID no. EPA-HQ-OW-2009-0297 (Drinking Water: Perchlorate Supplemental Request for Comments). Thank you.

September 18, 2009

Mr. Eric Burneson Office of Ground Water and Drinking Water Standards and Risk Management Division Environmental Protection Agency 1200 Pennsylvania Avenue, NW Washington, DC 20460

Re: Docket ID no. EPA-HQ-OW-2009-0297

Dear Mr. Burneson:

The Environmental Working Group (EWG) strongly supports the Environmental Protection Agency (EPA) establishing a drinking water standard for the rocket fuel ingredient perchlorate. This compound contaminates drinking water supplies nationwide at levels of concern for human health, providing the agency with a meaningful opportunity for human health risk reduction through a national primary drinking water rule:

- The EPA has reported finding perchlorate, a potent thyroid toxin, in public water systems in 28 states and territories and estimated that nearly 17 million people may be served by public water systems with at least one perchlorate detection > 4 ppb - The Centers for Disease Control and Prevention (CDC) have found perchlorate in the urine of nearly 3,000 Americans who were tested as part of a national biomonitoring study, indicating widespread exposure among the U.S.

population (Blount et al 2006a) - In infants and children, drinking perchlorate contaminated tap water can result in cumulative exposures that exceed the EPA's reference dose (RfD), even at tap water concentrations as low as 1 part per billion (ppb).

Recommendations

- EPA's own analyses show that infants under six months of age are exposed to enough perchlorate via food that additional exposure to perchlorate via tap water concentrations as low as 1 ppb can result in combined exposures that exceed the RfD. To protect these highly vulnerable individuals, EPA must set an MCL of less than 1 ppb for perchlorate in drinking water.

Response: See response to comment code 6120.

Commenter Name: Anila Jacob
Commenter Organization: Environmental Working Group (EWG)
EPA Document ID: EPA-HQ-OW-2009-0297-0499
EPA Comment ID: 28937
EPA Comment Code: 6120

Comment: Summary: There is a wealth of evidence from government and academic scientists that strongly suggests that infants and children not only have disproportionately high perchlorate exposure compared with adults, they are also more vulnerable to its toxic effects. Baseline perchlorate contamination of breast milk, powdered infant formula, and commonly consumed foods and beverages ensures that almost every infant and child in the U.S. will have multiple, daily sources of perchlorate exposure during critical periods of growth and brain development. However, for those children who live in states with perchlorate contamination of tap water, the additional exposure from the tap water can easily lead to cumulative exposures that exceed the agency's RfD. A decision by the agency to set an enforceable maximum contaminant level (MCL) of less than 1 ppb could benefit the health of millions of infants and children by decreasing cumulative perchlorate exposures.

Sincerely, Anila Jacob, M.D., M.P.H. Senior Scientist

Enc. Attachment 1

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Attachment 1:

Centers for Disease Control and Prevention's Responses to Questions for the Record From House Committee on Energy and Commerce

Response: See response to comment code 6120.

Commenter Name: Apparent Mass Mailing #9 - Group Unidentified)
EPA Document ID: EPA-HQ-OW-2008-0692-2366
EPA Comment ID: 29116
EPA Comment Code: 6120

Comment: Water Docket, EPA, Mailcode 2822T 1200 Pennsylvania Ave., NW Washington, DC 20460

To Whom It May Concern:

I urge you to reverse your decision and set a federal limit for perchlorate in drinking water. Perchlorate is a nationwide problem and has health impacts at lower levels than previously thought. Please protect public health, especially infants and children, by regulating perchlorate.

Response: Please see the response to comment code 6120.

Revisions: Page 3 (Comment ID 20759)

EPA Comment Code: 6125 Comments critical of preliminary determination (in the October 2008 FR Notice) specific to Washington Post article

Individual Comments
Commenter Name: J Richards
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0223
EPA Comment ID: 19835
EPA Comment Code: 6125

Comment: from Washington Post article

Last month, The Washington Post reported that White House officials had extensively edited the EPA's perchlorate rule-making documentation to remove scientific data highlighting some of the risks associated with the chemical, which has been found in water in 35 states. The Defense Department and Pentagon contractors who face legal liability stemming from rocket fuel contamination have lobbied for six years to avoid a federal drinking-water standard for perchlorate.

http://www.washingtonpost.com/wp- dyn/content/article/2008/10/03/AR2008100303280.html?nav=rss_business/government

This appears to be not only a medical but a political-moral issue.

Response: Please see the response to comment code 6110. EPA has reversed its October 2008 preliminary determination not to regulate perchlorate based upon a more direct evaluation of exposure to infants and developing children. In making today's final regulatory determination, EPA uses the criteria mandated by the 1996 SDWA Amendments. EPA has made its determination based upon a consideration of the best available peer reviewed science and data collected in accordance with accepted methods.

Commenter Name: Mary Beth Sullivan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0370
EPA Comment ID: 19844
EPA Comment Code: 6125

Comment: The Washington Post reported that "The GAO, which produced a 2005 report calling for a better federal tracking system for perchlorate, found that limited EPA data show the chemical compound has polluted the soil, groundwater and drinking water in 35 states and the District and has contaminated 153 public water systems in 26 states." The fact that there are some infants and toddlers in this country who drink formula using water contaminated by perchlorate is sinful. I have thyroid disease. I know how sluggish and foggy my mind becomes. I know how hard this disease is to diagnose.

We spend so many dollars on the military and "homeland security" to keep Americans "safe" from enemies. This perchlorate story is an example of the enemy within. The Washington Post also reports that, "A National Academy of Sciences panel prepared a risk analysis in 2005 that...came

under attack because two of the committee's members had financial ties to defense contractors that face legal liability because of perchlorate disposal." It seems to me that military contractors run this country. We know they hand out big bucks to decision makers to prevent creating regulation requiring them to clean up the mess they make.

Response: Please see the response to comment code 6110. EPA has reversed its October 2008 preliminary determination not to regulate perchlorate based upon a more direct evaluation of exposure to infants and developing children. In making today's final regulatory determination, EPA uses the criteria mandated by the 1996 SDWA Amendments. EPA has made its determination based upon a consideration of the best available peer reviewed science and data collected in accordance with accepted methods.

Commenter Name: Meghan Hendy
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1874
EPA Comment ID: 20759
EPA Comment Code: 6125

Comment: As reported in the Washington Post on September 22, 2008:

In the EPA's proposed rule, the administration assumes that perchlorate contamination of 15 ppb is safe. But its regulatory document states that "between 16,000 and 28,000 pregnant women" and 900,000 to 2 million Americans could be exposed to higher levels. The EPA document also finds that bottle-fed infants would be exposed to more than five times the level the National Academy of Sciences deemed safe -- 700 nanograms per kilogram of body weight per day -- if parents mix formula with drinking water containing perchlorate levels of 15 ppb.

Response: Please see the response to comment code 6110. EPA has reversed its October 2008 preliminary determination not to develop an NPDWR for perchlorate and now concludes, based on the analysis presented in this notice, that there is a substantial likelihood that perchlorate will occur in public water systems with a frequency and at levels of public health concern. Finally, EPA has determined that regulation of perchlorate presents a meaningful opportunity to reduce health risk for persons served by public water systems. EPA is initiating the development of a proposed NPDWR for perchlorate.

EPA Comment Code: 6130 Miscellaneous comments on the preliminary determination not to regulate (in the October 2008 FR Notice)

Individual Comments
Commenter Name: David Sparling, M.D., F.A.A.P.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0135
EPA Comment ID: 19722
EPA Comment Code: 6130

Comment: 2) The sources of perchlorate contamination of those public drinking water supplies should be identified and plans developed for decontamination of these sources or the development of alternative water supply sources not contaminated with perchlorate.

David Sparling, M.D., F.A.A.P. P.O. Box 88637 Steilacoom, WA 98388

dsparling@igc.org

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120. EPA will seek comment on any specific regulatory requirements as part of a proposed national primary drinking water regulation.

Commenter Name: Ed Thomas
Commenter Organization: National Rural Water Association (NRWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0163
EPA Comment ID: 20273
EPA Comment Code: 6130

Comment: Finally, NRWA feels that the issues raised by the aforementioned papers are of sufficient importance that it would be premature for the Agency to proceed with any of the possible scenarios for arriving at a perchlorate determination until these issues are resolved. For example, it is pointed out in the discussion of the evaluation of occurrence data and populations exposed (Table 5, page 24047) that this evaluation is very sensitive to the choice of an RSC and presumably to the occurrence data also. If the existing levels of contaminants are not known to any better accuracy than plus or minus a factor of 2 or more as is suggested by reference 1 above, it would not be good science to proceed with an analysis that is known to be sensitive to the value of such numbers.

Further we would encourage the agency to continue using and collecting data to support a "meaningful opportunity for public health protection" when determining if there is a clear benefit of regulating perchlorate. It is NRWA's belief that there is a need for more data to support this determination. There remain many uncertainties about the relative source contribution and the levels of perchlorate in urinary excretions. We believe that these issues along with the issues of affordability and compliance data variability must be appropriately addressed prior to the EPA Administrator making a determination regarding perchlorate, in accordance with Section 1412(b)(1)(A) of the 1996 SDWA Amendments, that "in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems."

We thank you for the opportunity to provide comments regarding this important matter.

Sincerely, Ed Thomas Ed Thomas

Electronic Attachments: 1. Phillips compliance data variability final.pdf 2. Rubin trade off health risk final.pdf

Response: EPA has made its determination based upon a consideration of the best available peer reviewed science and data collected in accordance with accepted methods related to perchlorate occurrence in drinking water, the presence of perchlorate in foods, and the health effects of exposure to perchlorate. Regarding the comment encouraging EPA to collect additional data to support the determination and to consider the papers the commenter provided, EPA believes there are sufficient data on which to evaluate the best available data to make the determination. EPA does not believe that affordability analysis is needed to make a regulatory determination. SDWA requires that EPA evaluate affordability for small systems and request comment at the time of proposing a national primary drinking water standard.

Commenter Name: Diane VanDe Hei
Commenter Organization: AMWA
EPA Document ID: EPA-HQ-OW-2008-0692-1525
EPA Comment ID: 20444
EPA Comment Code: 6130

Comment: National Academy of Sciences Review

In 2003, EPA asked the National Research Council (NRC) of the NAS to: * Assess the current state of the science regarding potential adverse effects of disruption of thyroid function by perchlorate and * Determine whether EPA's findings in its 2002 draft risk assessment were appropriate.

AMWA believes that regardless of the outcome of the final determination on perchlorate, the agency should commit to placing a similar question before the NAS for an answer by 2011.

If EPA's final decision is to regulate perchlorate, then the review of the science available since the 2005 NAS report should provide a good foundation on which to build a regulation. If the decision is not to regulate perchlorate for the present, then the review will either confirm the decision with respect to changes in the state of scientific knowledge or possibly point to the need to reassess the HRL and the regulatory determination.

Retention on the CCL

AMWA recommends that perchlorate be retained on the CCL or that some similar but less formal administrative action be taken so that changes in the science speaking to potential health effects and changes in occurrence continue to be captured and evaluated. AMWA recommends that in the final determination, EPA elaborate on how systems such as IRIS are used to keep risk and other pertinent contaminant information current and how it might be used to advantage in tracking any changes in perchlorate status.

Response: The Agency believes that a second review by the NAS would unnecessarily delay regulatory decision making for perchlorate. Therefore, EPA did not request additional NRC review of issues related to perchlorate. EPA has assessed recent best available data and has determined that regulation of perchlorate in drinking water systems presents a meaningful opportunity to reduce health risk for persons served by public water systems and has decided to regulate perchlorate in drinking water. See response to comment code 6120.

Regarding your recommendation that EPA ensure that changes in science related to potential health effects and changes in occurrence continue to be captured and evaluated, and elaborate on how systems such as IRIS are used to keep risk and other pertinent contaminant information current in tracking any changes in perchlorate status, because EPA has decided to regulate perchlorate in drinking water. EPA has found that perchlorate may have an adverse effect on human health. EPA has reversed its October 2008 preliminary determination not to develop an NPDWR for perchlorate and now concludes, based on the analysis presented in the final regulatory determination notice, that there is a substantial likelihood that perchlorate will occur in public water systems with a frequency and at levels of public health concern. Finally, EPA has determined that regulation of perchlorate presents a meaningful opportunity to reduce health risk for persons served by public water systems. The Safe Drinking Water Act requires EPA to review each National Primary Drinking Water Regulation (NPDWR) at least once every six years and revise them, if appropriate. The purpose of the review, called the Six-Year Review, is to identify those NPDWRs for which current health effects assessments, changes in technology, and/or other factors provide a health or technical basis to support a regulatory revision that will maintain or strengthen public health protection. EPA will address changes in the science and occurrence at that time.

Commenter Name: Laurence Scudder
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1581
EPA Comment ID: 20561
EPA Comment Code: 6130

Comment: I urge the U.S. Environmental Protection Agency to reverse its preliminary determination on setting a regulation for perchlorate in drinking water. It is my understanding that the effects of levels of perchlorate in our drinking water have not been fully researched. Until said testing has been performed, I believe it is inconclusive to set a standardized acceptable level of perchlorate in our drinking water. Most of all because perchlorate affects the thyroid gland almost exclusively. This fact targets our children and unborn children as their thyroids are responsible for their growth and development not just metabolism as in adults. Thank you for your time and strongly consider my plea. Sincerely, Laurence Scudder

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Samuel A. L. Perry
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1604
EPA Comment ID: 20563
EPA Comment Code: 6130

Comment: While I think perchlorate should be regulated, I would support a reduced monitoring framework for those water systems that have samples less than half any MCL that eventually gets developed. I also understand that monitoring costs may drop significantly as new analytical platforms are developed.

Sincerely, Samuel A. L. Perry, P.E.

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120. Specific regulatory requirements for public water systems (including monitoring) will be presented for public comment with the proposed NPDWR.

Commenter Name: James Taft
Commenter Organization: Association of State Drinking Water Agencies
EPA Document ID: EPA-HQ-OW-2008-0692-1527
EPA Comment ID: 20634
EPA Comment Code: 6130

Comment: November 10, 2008

Comment Clerk Docket EPA-HQ-OW-2008-0692 Water Docket Environmental Protection Agency Mail Code: 2822T 1200 Pennsylvania Ave., NW. Washington, DC 20460

Dear Sir:

In response to the notice in the Federal Register of October 10, 2008 (Volume 73, Number 198) the Association of State Drinking Water Administrators (ASDWA) is offering comments to the U.S. Environmental Protection Agency (EPA) on the Preliminary Regulatory Determination on Perchlorate. ASDWA is the professional Association that represents the collective interests of the nation's state drinking water programs responsible for implementation of the Federal Safe Drinking Water Act.

EPA's regulatory development activities are very important to states. Although some states have the expertise and resources to conduct their own evaluations of contaminant risks and may set their own, more stringent regulatory controls, most states rely on the EPA to determine which contaminants should be regulated in drinking water and at what levels. It is critical that these determinations are based on sound science and accomplished through a transparent process with appropriate input from all interested parties, especially states. This is especially true in the case of perchlorate, since this contaminant has garnered extensive public and political interest in the last few years.

ASDWA appreciates the opportunity to provide the perspective of states on the Agency's preliminary determination for perchlorate. States are generally in favor of EPA's decision not to regulate, but there are some states that do favor national regulation of perchlorate, especially those who have already set their own standard. The Agency should expect direct comments from some of these states. We do have a few recommendations to offer related to the perchlorate decision about tools and information that we believe would benefit to all states. These recommendations do not include a recommendation to regulate, but they do go beyond the norm.

Regardless of EPA's regulatory decision, states will need to act - Even if EPA does not adopt a national regulation of perchlorate, the public will likely demand a response to detections of elevated levels of perchlorate - particularly, in light of the notoriety associated with this contaminant. The occurrence data may not support regulation of perchlorate, but the data do show that there are a significant number of water sources where perchlorate was detected, and at least a few where the levels are a public health concern. Because the decision not to regulate was based on a low national number of detects at levels of concern and not a lack of health effects, there is still a need for action in some cases, even if a national standard is not justified. In states where there are detections of perchlorate at levels of concern, drinking water programs need to be able to respond appropriately so that public health can be protected. At a minimum, states will need to assist individual water systems with the specific actions needed to control perchlorate. Information is needed from EPA on risk characterization and risk management as well as treatment options and alternative control measures to support state efforts. In some cases, a state may decide that perchlorate is common enough in their source waters that they are interested in developing statewide control measures, whether it is a formal monitoring program or a state specific MCL. We believe the Agency has data and expertise that can help support these actions.

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120. EPA will provide further risk characterization and risk management information as part of the national primary drinking water standard.

Commenter Name: Lewis Zediana
Commenter Organization: Tewksbury Water Department
EPA Document ID: EPA-HQ-OW-2008-0692-1670
EPA Comment ID: 20669
EPA Comment Code: 6130

Comment: Please find attached my comments on this subject.

Perchlorate should not be dropped from the list. Montioring can be adjusted by allowing waivers while taking into consideration the surrounding area and chances of contamination. However more protection can be afforded to the populace by expanding the monitoring program to the effluent of wastewater plants. Which as by our experience can release Perchlorate passed inot the system..

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120. EPA intends to present specific regulatory requirements for public water systems (including monitoring) for public comment with the proposed NPDWR. This action does not address waste water discharges.

Commenter Name: Lyndsey Crum
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1732
EPA Comment ID: 20679
EPA Comment Code: 6130

Comment: While I support the EPA's desire to not promulgate NPDWR for perchlorate for the reason above, I am concerned about the health implications this will have for the sensitive subpopulations of infants, pregnant women and those likely to become pregnant. Although the

connection between perchlorate and thyroid related health and cognitive defects is not conclusion, the EPA presents evidence that suggest such a link could exists. The possibility should be sufficient to warrant clearer, quantitative research targeting these populations, particularly in industrial communities where perchlorate could enter the public water supply.

In addition to a targeted study, the agency should consider the costs of not regulated perchlorate versus the possible treatment costs associated with thyroid conditions. Regulatory cost saving should not outweigh the cost of prevention.

Although the EPA is not required to promulgate NPDWR for perchlorate, should it conduct additional research, in which that research produces a strong health risk concern; EPA should create a NPDWR to address regulation needs. The regulation could be enforcing only when the state health agency has not already passed a sufficient state public drinking water regulation.

Lyndsey Crum lcrum10@law.du.edu

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120. To do so, EPA used the best available peer-reviewed science and does not think that an additional targeted study is necessary at this point. EPA intends to develop a proposed NPDWR, at which time EPA will analyze, among other things, quantifiable and nonquantifiable health risk reduction benefits as well as costs of a rule, the effects of perchlorate on the general population and specific life stages, and other relevant factors with respect to the degree and nature of the risk. See 42 USC 1412(b)(3)(C).
Because EPA has decided to regulate perchlorate in drinking water the Safe Drinking Water Act requires EPA to review each National Primary Drinking Water Regulation (NPDWR) at least once every six years and revise them, if appropriate. The purpose of the review, called the Six-Year Review, is to identify those NPDWRs for which current health effects assessments, changes in technology, and/or other factors provide a health or technical basis to support a regulatory revision that will maintain or strengthen public health protection. EPA will evaluate changes in the science and occurrence at that time.

Commenter Name: Richard Weaver
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1868
EPA Comment ID: 20752
EPA Comment Code: 6130

Comment: Management,

Clean Water Action:

Please consider offering surveyed citizens more comprehensive information on the perchlorate in drinking water. Please also offer them either a pre-written form or guideliness on writing to the EPA on this issue. Thank you

Richard Weaver

Response: EPA has provided comprehensive information through three Federal Register notices and has provided instructions on how to provide comments. Furthermore, pursuant to 42 USC 300(b)(3)(B), EPA intends to publish a document in support of its NPDWR that specifies, to the extent practicable-- (i) each population addressed by any estimate of public health effects; (ii) the expected risk or central estimate of risk for the specific populations; (iii) each appropriate upper-bound or lower-bound estimate of risk; (iv) each significant uncertainty identified in the process of the assessment of public health effects and studies that would assist in resolving the uncertainty; and (v) peer-reviewed studies known to the Administrator that support, are directly relevant to, or fail to support any estimate of public health effects and the methodology used to reconcile inconsistencies in the scientific data.

Commenter Name: Rebecca Downey
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1888
EPA Comment ID: 20774
EPA Comment Code: 6130

Comment: I urge you to reconsider any decisions on this important matter until proper analysis of all studies, including those that contradict industry studies, have been properly assessed and considered.

Sincerely,

Rebecca Downey

Rebecca Downey sent this message via Congress.org, which uses the Capwiz.XC system. Congress.org is a free public service of Capitol Advantage and Knowlegis, LLC. You may access Congress.org here: http://congress.org

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120. This determination was based on analysis of the best available science.

Commenter Name: Lucy Allen
Commenter Organization: Pacific Institute
EPA Document ID: EPA-HQ-OW-2008-0692-1770
EPA Comment ID: 20927
EPA Comment Code: 6130

Comment: Without an enforceable federal standard, the Department of Defense, which is a primary user of perchlorate in the U.S., will perform remediation efforts according to a patchwork of state and agency guidelines. According to the EPA, approximately 90 percent of perchlorate produced in the United States is for defense activities and NASA.[FN7: EPA (2007). Perchlorate. Environmental Protection Agency, Federal Facilities Restoration and Reuse. Retrieved Oct. 24, 2008 from http://www.epa.gov/fedfac/documents/perchlorate.htm.] Recognizing perchlorate contamination is a defense-related hazardous waste issue with significant potential impact on human health, the Department of Defense (DOD) designated perchlorate as an emerging contaminant and has taken some action to clean up contamination, mostly in the form of responding to requests made by the EPA and states-requests that relied on piecing together statutes, regulations, and the

power of oversight agencies.[FN8: GAO (2007). Department of Defense Activities Related to Trichloroethylene, Perchlorate, and Other Emerging Contaminants. Government Accountability Office. July, 2007. Retrieved October 24, 2008 from http://www.gao.gov/new.items/d071042t.pdf.] While the DOD is responsible by law for remediation of contaminants regulated by the EPA or the state, its responsibility for what it classifies as "emerging contaminants" is not clearly defined.

In 2006, the DOD adopted its own management policy in which they are to comply with state or federal standards, whichever is most stringent. According to this policy, in the absence of state or federal standards, the DOD will manage its control action using 24 parts per billion (ppb) as the level of concern. Because a federal standard has not yet been established, the DOD must use state regulations to guide its remediation efforts. But while a handful of states have nonregulatory perchlorate-level guidelines, only two states-Massachusetts and California-have set enforceable perchlorate drinking- water standards (1 ppb and 6 ppb respectively). Perchlorate contamination and its potential adverse health impacts, however, is obviously a multistate issue.[FN9: GAO 2007 finds federal and state agencies have found perchlorate in groundwater, surface water, soil, or public drinking water systems at almost 400 sites representing over 37 states, in concentrations that ranged from 4 parts per billion (ppb) to more than 3.7 million ppb. http://www.gao.gov/new.items/d07797t.pdf] Without a federal standard, not only will the DOD have to overcome the difficult challenge of performing remediation efforts according to varied guidelines, but states that currently lack their own enforceable standards and have known sources of perchlorate may be left with remediation efforts based on the DOD's 24 ppb management standard.

In the absence of a federal standard, remediation efforts by EPA and state officials of public drinking water systems contaminated by perchlorate have been shown to be nonexistent. DOD remediation efforts are not alone in their need for guidance from a federal perchlorate standard-cleanup of perchlorate in public drinking water systems has been shown to be nonexistent without a federal standard. According to research done by the GAO, "EPA and state officials told us they had not cleaned up contaminated public drinking water systems, principally because there was no federal drinking water standard or specific federal requirement to clean up perchlorate."[FN10: GAO. (2007). Perchlorate: EPA Does Not Systematically Track Incidents of Contamination. Retrieved Oct 27, 2008 from http://www.gao.gov/new.items/d07797t.pdf.]

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20989
EPA Comment Code: 6130

Comment: DETAILED COMMENTS

1. EPA has made a preliminary determination not to set a health standard for perchlorate without reviewing or considering peer review and public comments on key pieces of evidence which it relies upon for its determination.

As EPA announced in its preliminary determination on perchlorate, the Agency is planning to issue a final determination by December 2008. However, NRDC has learned that the PBPK peer review reports of the staff report have only recently been submitted to EPA and were not incorporated into EPA's analysis in making its regulatory determination. Furthermore, NRDC has learned that EPA has solicited peer review comments on the HRL itself, and to date, is still awaiting those comments. EPA should not proceed with any decision on perchlorate until all the peer review reports have been submitted to EPA, reviewed by EPA scientific staff and managers, and made available for public scrutiny.

If EPA finalizes its preliminary determination, in the absence of strong state drinking water standards for perchlorate, the HRL will provide the only guidance for Superfund cleanup levels and health advisories for perchlorate. The importance of the HRL if EPA chooses not to regulate perchlorate underscores the importance that it be fully peer reviewed and those comments be made available to the public before EPA finalizes its determination. There is no justification for EPA's apparent intent to race ahead with a decision not to set a health- standard for perchlorate, and to rely upon an inadequate health reference level, prior to receiving, considering, and responding to both peer review and public comment. Failing to give these comments sufficient consideration in making its final determination would render EPA's final action arbitrary and capricious.

Response: All the peer review reports have been submitted to EPA, reviewed by EPA, and made available for public scrutiny. EPA has considered the results of the peer review reports in reaching the determination it announces today to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Dawn M. Lee
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2117
EPA Comment ID: 21968
EPA Comment Code: 6130

Comment: Dawn M. Lee 1219 Severnview Dr. Crownsville, MD 21032

Water Docket, EPA Mailcode 2822T 1200 Pennsylvania Ave. Washington, DC 20460

Re: EPA-HQ-OW-2008-0692

I am writing to express my concerns regarding the issue of perchlorate levels in our drinking water in the United States. I feel this chemical should be further studied and monitored in our drinking water and water tables, and eliminated as much as possible. For the future of our children and their children, please continue to study the effects of perchlorate do not allow this chemical to remain uncontrolled in our drinking water.

Thank you, Dawn M. Lee

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120. To do so, EPA used the best available peer-reviewed science. EPA intends to present specific regulatory requirements for public water systems (including monitoring) for public comment with the proposed NPDWR.

Commenter Name: Carrie Manion
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2121
EPA Comment ID: 21997
EPA Comment Code: 6130

Comment: 2194 Dairy Farm Road Gambrills, MD 21054

November 20, 2008

Environmental Protection Agency Water Docket 1200 Pennsylvania Ave. Washington, DC

RE: EPA-HQ-OW-2008-0692

Dear Sirs/Madam:

A recent online review of information about perchlorate proved very interesting. It seems that several states are imposing limitations on the presence of perchlorate in water; however the recommended "safe" levels are inconsistent.

I feel that in order for the public to be protected by the potential risks associated with ingesting perchlorate, the EPA should conduct further, in depth studies into the actual ramifications of this chemical.

Instituting a drinking water regulation cannot be done until accurate, authoritative research into the health impacts is conducted.

I look forward to seeing the results of such tests in a timely manner.

Carrie Manion Resident of Anne Arundel County, Maryland

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120. To do so, EPA used the best available peer-reviewed science. EPA intends to conduct further analyses, pursuant to the requirements of 42 USC 300g-1(3)(C)(i), in promulgating the NPDWR with a maximum contaminant level.

Commenter Name: Andy Burgess
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2217
EPA Comment ID: 22417
EPA Comment Code: 6130

Comment: All Americans deserve healthy and clean drinking water. The EPA should not finalize this decision until the scientific review is complete and should make decisions that are consistent with the agency's own scientists. Contrary to your claims, protecting the health of young children is indeed a "meaningful opportunity for health risk reduction."

Response: All the peer review reports have been submitted to EPA, reviewed by EPA, and made available for public scrutiny. EPA has considered the results of the peer review reports in reaching the determination it announces today to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Rose Lernberg
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2246
EPA Comment ID: 22429
EPA Comment Code: 6130

Comment: Please do not finalize this decision until the scientific review is complete. Please make decisions that are consistent with the agency's own scientists.

Sincerely, Rose Lernberg 831 Balra Drive E1 Cerrito, CA 94530

Response: All the peer review reports have been submitted to EPA, reviewed by EPA, and made available for public scrutiny. EPA has considered the results of the peer review reports in reaching the determination it announces today to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Susanna Sayre
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2310
EPA Comment ID: 24991
EPA Comment Code: 6130

Comment: Water Docket Environmental Protection Agency Mailcode 2822T,1200 Pennsylvania Avenue Washington, DC 20460

ATTN: Docket ID No. EPA-HQ-OW-2008-0692

To whom it may concern:

Perchlorate contamination in drinking water is a nationwide problem. As noted recently by the EPA's own Scientific Advisory Board, perchlorate's widespread occurrence in drinking water and its well-documented toxicity to humans make it vital to have the best scientific evidence available in making a determination as to whether or not perchlorate levels should be regulated. Given its potential for posing significant risks to human health, I urge the EPA to delay final action on its decision not to set a federal drinking-water standard for perchlorate. I support a national primary drinking water regulation governing perchlorate levels to protect public health.

Yours sincerely, Susanna Sayre 19005 Bloomfield Rd. Olney, MD 20832

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Michael Sayre

Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2327
EPA Comment ID: 25009
EPA Comment Code: 6130

Comment: November 10, 2008 Water Docket Environmental Protection Agency Mailcode 2822T, 1200 Pennsylvania Avenue Washington, DC 20460

ATTN: Docket ID No. EPA-HQ-OW-2008-0692

To whom it may concern:

Perchlorate contamination in drinking water is a nationwide problem. As noted recently by the EPA's own Scientific Advisory Board, perchlorate's widespread occurrence in drinking water and its well-documented toxicity to humans make it vital to have the best scientific evidence available in making a determination as to whether or not perchlorate levels should be regulated. Given its potential for posing significant risks to human health, I urge the EPA to delay final action on its decision not to set a federal drinking-water standard for perchlorate. I support a national primary drinking water regulation governing perchlorate levels to protect public health.

Yours sincerely, Michael Sayre 19005 Bloomfield Rd. Olney, MD 20832

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: James D. Taft
Commenter Organization: Association of State Drinking Water Administrators
EPA Document ID: EPA-HQ-OW-2009-0297-0525
EPA Comment ID: 28496
EPA Comment Code: 6130

Comment: Atttached are the comments of the Association of State Drinking Water Administrators on the request for additional comments on the regulation of perchlorate (FR Vol. 74, No. 159). Additional comments are being submitted directly by states.

Attachment

September 24, 2009 Comment Clerk Docket EPA-HQ-OW-2009-0297 Water Docket Environmental Protection Agency Mail Code: 2822T 1200 Pennsylvania Ave., NW. Washington, DC 20460

Dear Sir:

In response to the notice in the Federal Register of August 19, 2009 (Volume 74, Number 159) the Association of State Drinking Water Administrators (ASDWA) is offering comments to the U.S. Environmental Protection Agency (EPA) on the Perchlorate Supplemental Request for Comments. ASDWA is the professional Association that represents the collective interests of the nation's state drinking water programs responsible for implementation of the Federal Safe Drinking Water Act.

EPA's regulatory development activities are very important to states. Although some states have the expertise and resources to conduct their own evaluations of contaminant risks and may set their own, more stringent regulatory controls, most states rely on the EPA to determine which contaminants should be regulated in drinking water and at what levels. It is critical that these determinations be based on sound science and accomplished through a transparent process with appropriate input from all interested parties, especially states. This is particularly true in the case of perchlorate, since this contaminant has garnered extensive public and political interest in the past few years. We appreciate that EPA is sharing its assessment of health risk and occurrence data and requesting additional comment as important regulatory decisions are considered.

As we noted in our comments on EPA's preliminary decision on perchlorate regulation in October 2008, states were generally in favor of EPA's preliminary decision not to regulate, but there are some states that do favor national regulation of perchlorate, especially those who have already set their own standard. In that response, we did recommend some tools and information that we believed would benefit all states. Our comments today will address some of the questions in the Agency's August 19th request for comments, but also reiterate some of the recommendations in our previous letter, where appropriate.

Response: Please see the response to comment code 6110.

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 28748
EPA Comment Code: 6130

Comment: In summary, the NDEP believes the EPA should develop a national primary drinking water standard for perchlorate using updated, appropriate, and complete data sets; defensible analysis; and scientific approaches. The States and general public place a tremendous amount of trust in the EPA to make credible decisions. Consequently, we trust the EPA will thoughtfully consider our comments and those submitted by other entities during its current evaluation. Much more significant public health benefit is achievable and at a much lower cost by targeting iodine-deficient individuals through existing public health programs and correcting the iodine deficiencies through adjusted diets, use of supplements, and implementation of educational programs. These concepts are not new, yet they have not been addressed in a meaningful way. Congress is capable of funding such programs and should be requested to do so in the near term.

Sincerely, Tom Porta, Deputy Administrator Nevada Division of Environmental Protection

Tp/tjc cc Jennifer Carr, P.E., CEM, Chief, Bureau of Safe Drinking Water, Nevada Division of Environmental Protection, 901 S. Stewart Street, Suite 4001, Carson City, NV 89701-5249 Darrel Osterhoudt, Regulatory Affairs Manager, Association of State Drinking Water Administrators, 1401 Wilson Blvd., Suite 1225, Arlington, VA 22209 Kay Brothers, Deputy General Manager, SNWA Engineering/Ops, Southern Nevada Water Authority, 100 City Parkway, Suite 700, Las Vegas, NV 89106 Dr. Mic Stewart, Manager, Water Quality Section, Metropolitan Water District of Southern California, 700 North Alameda Street, Los Angeles, CA 90012 Marie Pearthree, Assistant General Manager, Central Arizona Water Conservation District, PO Box 43020, Phoenix, AZ 85080-3020

Brenda Pohlmann, Environmental Programs Manager, City of Henderson, PO Box 95050, Henderson, NV 89009 Susan Crowley, Tronox, LLC, PO Box 55, Henderson, NV 89009 Jeff Gibson, AMPAC, 3883Howard Hughes Parkway, Suite 70, Las Vegas, Nevada 89109

Response: Please see the response to comment ID 28857 under comment code 6110.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28795
EPA Comment Code: 6130

Comment: However, even when basing its decision upon this unacceptably high RfD, EPA's preliminary determination not to regulate perchlorate would still expose hundreds of thousands of children and infants to unsafe levels of perchlorate.

Response: EPA has determined to regulate perchlorate in drinking water. See response to comment code 6120. For further information about the RfD for perchlorate, please see the response to comment ID 28927 under comment code 2110.

EPA Comment Code: 6140 Additional new literature and information for EPA to consider when making a regulatory determination

Individual Comments
Commenter Name: Bill Connick
Commenter Organization: University of Cincinnati
EPA Document ID: EPA-HQ-OW-2009-0297-0190
EPA Comment ID: 28387
EPA Comment Code: 6140

Comment: Dear Sir,

We have developed a new method for detection of perchlorate in aqueous solution with remarkably high selectivity. The method is likely to be low- cost relative to exisiting approaches (e.g., those described at http://www.clu-in.org/contaminantfocus/default.focus/sec/perchlorate/cat/Overview/) and suitable for field work. We are preparing a manuscript for submission to the Journal of the American Chemical Society describing the discovery. I expect the document will be submitted within 10 days.

The science described in that account is covered by a provisional patent. We have recently made some significant improvements which will greatly increase the sensitivity. If this sounds relevant, please feel free to contact me.

Professor Bill Connick University of Cincinnati (513)-556-0148 bill.connick@uc.edu

Regards, Bill

Response: EPA cannot evaluate methods that have not been peer reviewed. However, EPA will evaluate the best available, peer reviewed literature as the NPDWR is developed.

Commenter Name: Richard Nieuwenhuis
Commenter Organization: New Jersey Farm Bureau (NJFB)
EPA Document ID: EPA-HQ-OW-2009-0297-0665
EPA Comment ID: 28533
EPA Comment Code: 6140

Comment: October 8, 2009

Water Docket Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Avenue Washington, DC 20460

RE: Perchlorate Supplemental Request for Comments (Docket ID No. EPA-HQ- OW-2009-0297)

Dear Sir/Madam:

The New Jersey Farm Bureau (NJFB) is a 13,000 member organization which represents New Jersey agricultural producers and enterprises at all levels of government. We thank the Environmental Protection Agency (EPA) for the opportunity to provide comments on the above referenced docket regarding alternative approaches to the interpretation of scientific data relevant to establishment of a national primary drinking water regulation for perchlorate.

We believe that the approaches EPA described in the August 19, 2009 Federal Register deviate from long-established methods by which EPA has analyzed scientific and technical data. We are concerned that development of an overly conservative standard for perchlorate, that is not based on comprehensive, peer- reviewed science and an appropriate risk-based assessment could unintentionally lead to unjustified food scares associated with a wide variety of agricultural commodities. Food scares of this nature could deter people away from consuming foods which the Food and Drug Administration (FDA) encourages people to eat more of due to their nutritional benefits and which the FDA has deemed critical to the health and development of children. Furthermore, we are concerned about the economic impacts associated with such food scares.

Response: SDWA requires the consideration of sensitive subpopulations in developing NPDWRs. EPA exposure assessment policy has evolved to provide tools and policies consistent with the concern for all life stages. See responses to comments IDs 28813 and 28677 under comment code 6140.

Commenter Name: Stephen Haterius
Commenter Organization: National Association of State Departments of Agriculture (NASDA)
EPA Document ID: EPA-HQ-OW-2009-0297-0664
EPA Comment ID: 28548
EPA Comment Code: 6140

Comment: We remain very concerned that the approaches EPA outlined in the August 19 Federal Register will significantly-and unnecessarily-impact American agricultural production and foreign trade. Because perchlorate is naturally occurring at low levels in a number of agricultural products, it is imperative that EPA's regulatory determination be based upon a sound scientific approach that protects public health without unnecessarily creating concerns about the safety of agricultural products that are vital to a healthy diet. This is particularly important in light of the fact that the risks associated with perchlorate can be easily avoided by the consumption of sufficient iodine-rich foods or iodine supplements by a specific subset of the population.

As we detailed in previous comments, an overly conservative perchlorate standard that is not based on sound, peer-reviewed science and an appropriate risk-based assessment could unintentionally lead to unjustified food scares on a wide variety of fresh fruits, vegetables, and dairy products. Even though EPA's current action is intended only to explore alternative approaches to analyzing data, the additional alternatives under consideration could result in health reference levels which are much lower than the level identified in the October 2008 notice. NASDA is concerned that this kind of standard would likely lead to inaccurate consumer perceptions and confusion about perchlorate in agricultural products. The ramifications of this kind of food scare would have devastating impacts on agricultural producers and rural communities. For example, a study by Arizona State University indicates that a prolonged food scare involving winter lettuce could result in a negative economic impact of over $5 billion.

Moreover, EPA's actions could have significant impacts on American producers' access to foreign markets. The agricultural products impacted by this issue represent nearly $70 billion in export opportunities. Because other countries frequently cite food safety concerns as justifications to erecting trade barriers to American agricultural products, an overly conservative perchlorate standard that is not based on sound, peer-reviewed science and an appropriate riskbased assessment would likely lead to the imposition of unfair and economically devastating trade restrictions by America's trading partners.

Response: See responses to comments IDs 28813 and 28677 under comment code 6140.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0653
EPA Comment ID: 28559
EPA Comment Code: 6140

Comment: Further conservatism (i.e. more stringent assumptions) concerning hazard or exposure beyond central tendencies in the existing data sets is not justified. To follow a precautionary principal in setting further restrictions in this case is both arbitrary and capricious. Further, without a clear basis for protecting public health, the Agency will cause public and private water providers to expend energy to remove perchlorate from water supplies that already protect their consumers. The Agency has failed to estimate the carbon emissions and cost that this unnecessary removal, probably through dedicated reverse osmosis systems, will cost the American public in higher water rates and carbon emissions. The Agency has provided no data on the feasibility of removing perchlorate below the preliminary guidance level. In doing so, costs must be estimated for both the construction capital costs and based on energy expenditures which are an ongoing annual cost rather than a one-time capital cost. Such ongoing costs must be considered for the life of the project.

Response: See response to comment ID 28813 under comment code 6140.

Commenter Name: Sonia Salas
Commenter Organization: Western Growers Association on behalf of several California agriculture groups
EPA Document ID: EPA-HQ-OW-2009-0297-0652
EPA Comment ID: 28677
EPA Comment Code: 6140

Comment: We are further concerned that the food scares which will follow from setting a regulatory threshold below the existing natural background level of perchlorate in the environment will significantly disadvantage agricultural exports. Agricultural commodities make up a significant portion of all U.S. food exports. Given the long history of our Asian trading partners taking retaliatory actions for what they deem to be U.S. protectionism -- we are particularly concerned in light of the Obama Administration's recent announcement to impose tariffs on Chinese tire manufacturers -- a regulatory determination which does not take into consideration the presence of naturally occurring perchlorate will provide an unfortunate opportunity for the Chinese government to make good on their threats to punish U.S. agricultural exports.

Response: EPA is aware of the need to communicate clearly the implications of the NPDWR that is developed. The NPDWR as currently envisioned assumes that no change will be required to the food supply. Adjustment to perchlorate exposure will be made in the drinking water supply, assuming that the food supply remains in its current state with regard to perchlorate.

Commenter Name: Robert Callahan
Commenter Organization: California Chamber of Commerce (CalChamber)
EPA Document ID: EPA-HQ-OW-2009-0297-0666
EPA Comment ID: 28693
EPA Comment Code: 6140

Comment: Please see the attached comment letter regarding the perchlorate supplemental request for comments. Thank you.

Robert Callahan California Chamber of Commerce

October 8, 2009

Ms. Lisa P. Jackson Administrator Environmental Protection Agency 1200 Pennsylvania Avenue, NW Washington, DC 20460

SUBJECT: EPA-HQ-OW-2009-0297, "Drinking Water: Perchlorate - Supplemental Request for Comments"

Dear Ms. Jackson:

The California Chamber of Commerce (CalChamber) wishes to express our concern with the federal Environmental Protection Agency's (EPA) interpretation of the scientific data relevant to a regulatory determination for perchlorate in drinking water. While it is imperative to set public health standards, especially where a specific threat exists, there is no rationale for establishing lower standards or for rushing to a regulatory decision unsupported by scientific information.

Perchlorate is found naturally throughout the water environment in the 0.5 to 15 parts per billion range. The United States Geological Survey and other researchers have also measured perchlorate in rain, geologic formations, and rivers and aquifers throughout the United States. Five decades of scientific investigation, including a landmark National Academy of Sciences review, result in a clear and consistent conclusion: low levels of perchlorate are not dangerous to public health.

We strongly believe that an unnecessarily lower standard would limit the flexibility of the water supply system. Curbs on water supplies, especially during a water emergency, would impact local economies and job markets, as plans for new housing areas and business centers are postponed or cancelled due to lack of available water. Current residential areas and businesses could also be forced to endure unnecessary water shortages, water rationing, rate hikes and other consequences.

In light of this, it seems clear that the alternatives proposed by EPA are not justifiable considering the significant economic costs that would be incurred without corresponding benefits to public health. Please keep these considerations in mind as the EPA determines additional approaches to interpreting perchlorate level data.

Sincerely, Robert Callahan Policy Advocate RC:fg

Response: See response to comment ID 28813 under comment code 6140. As explained elsewhere in this response to comments document (comment ID 28863 under comment code 2110), EPA believes that the RfD derived by the NRC is the best health assessment available for assessing risk to perchlorate.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2009-0297-0647
EPA Comment ID: 28719
EPA Comment Code: 6140

Comment: Appendix 1

A first step towards a possible link perchlorate-organohalogens-TH

It has been shown that chlorine-based disinfectants such as those found in drinking water oxidize to perchlorate as a disinfection by-product (DBP). This is, for example, why Massachusetts doubled its MCL from 1 to 2 ppb, because otherwise health-protecting chlorination of drinking water and swimming pools with bleach would have to be curtailed. Is this oxidation of perchlorate from bleach (hypochlorite and hypochlorous acid) and other chlorine derivates significant in comparison with daily intake of perchlorate?

According to the Blount study (based on the NHANES survey data) the average urinary perchlorate level in the population is 2.84ug/l which is roughly equivalent to an oral dose of 0.04 ug/kg-day. This corresponds with drinking water of 1.4 ppb. Massachusetts' MCL was based on data that showed that about 0.5 ppb perchlorate originated from bleach alone[FN16: -Massachusetts Department of Environmental Protection. Perchlorate: Draft Toxicological Profile and Health Assessment. 2004. - Occurrence of Perchlorate in Sodium Hypochlorite, Journal American Water Works Association (AWWA), Nov. 2008.]. Therefore about 1/3 of the average daily intake of perchlorate would be due to bleach oxidation alone, which is substantial and which shows that chlorine could be a significant source of low level perchlorate.

Bleach is used ubiquitously, as for example in water purification stations, paper mills, drinking water and for many other applications. Other potential sources of perchlorate as a DBP are other chlorine derivates such as chlorine gas and chloramine. On the other hand other DBPs originate from the reaction of chlorine based disinfectants with organic matter (waste) to form organochlorides[FN17: Gary A. Boorman, Vicki Dellarco, June K. Dunnick, Robert E. Chapin, Sid Hunter, Fred Hauchman, Hank Gardner, Mike Cox, and Robert C. Sills. Drinking Water Disinfection Byproducts: Review and Approach to Toxicity Evaluation. Environmental Health Perspectives Supplements, February 199, Volume 107, Number S1.]. What could be one of the possible pathways that link perchlorate to organochlorides such as PCBs via chlorine?

According to EPA the building block for organochlorides is chlorophenol, and chlorophenols are produced from the organic matter found in used water when it reacts with chlorinated disinfectants[FN18: Environmental Protection Agency, EPA/600/P-03/002F).An Inventory of

Sources and Environmental Releases of Dioxin- Like Compounds in the United States for the Years 1987, 1995 and 2000. Federal Register: December 1, 2006 (Volume 71, Number 231)] Page 69564-69565] Occurrence of Perchlorate in Sodium Hypochlorite, Journal American Water Works Association(AWWA), Nov. 2008] (phenol is benzene with a hydroxyl group and PCBs are basically 2 chlorinated benzene rings). Those DBPs are found back in the drinking water leaving the water purification plants.

Therefore, this is one example of the possible link between very low levels of perchlorate and TH affecting substances: chlorine based disinfectants such as bleach, Cl2 and chloramines evolve to perchlorate in one way and to phenols, PCBS and other organochlorides including dioxin-like compounds in another way. [Chloramines, besides being an added disinfectant, can also be formed as a reaction product of bleach with ammonia, itself amply present in used water (see ref. 15)].

Response: EPA is aware of the link between perchlorate and hypochlorite/hypochlorous acid. This issue, and those related to other possible transformation products, will be considered in the context of NPDWR development.

Commenter Name: Jennifer Sass
Commenter Organization: Natural Resources Defense Council (NRDC)
EPA Document ID: EPA-HQ-OW-2009-0297-0412
EPA Comment ID: 28813
EPA Comment Code: 6140

Comment: A Final MCL Below 1 ppb is Both Technologically and Economically Feasible

U.S. EPA's Method 314 approved ion chromatography detection protocol, for example, routinely detects perchlorate pollution at levels of 0.2ppb and the State of Massachusetts has established a 'reportable concentrations level for perchlorate of 2 ppb.[FN66: Thorne, Philip G. Field Screening Method for Perchlorate in Water and Soil, ERDC/CRREL Technical Report 04-8, 36 pp, Apr 2004.],[FN67: "Final Changes to the Massachusetts Contingency Plan -310 CMR 40.0000," downloaded from http://www.mass.gov/dep/cleanup/laws/perchlorate-310CMR40-07282006.pdf, November 2 2006.] Ion exchange technology is able to treat perchlorate contamination to levels considerably below 1 ppb. Treatment systems operating on perchlorate- impacted wells owned by Aquarion Water Company in Massachusetts, for example, treat wells to below 1 ppb.[FN68: "US Filter Recovery Services," downloaded from www.usfilter.com, November 2 2006.]

Economically, the cost of complying with a perchlorate MCL less than 1 ppb for the City of Rialto - one of the most impacted water systems in California - for example will be zero after cleanup costs are recovered from identified responsible parties. A complete economic feasibility study should also include an analysis of the costs associated with healthcare and lost work resulting from illnesses associated with perchlorate contaminated water.

Response: EPA agrees that analytical methods and treatment techniques are available to address increasingly smaller concentrations of perchlorate. As the NPDWR is developed, economic feasibility will be evaluated in support of identifying an MCL.

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)

EPA Document ID: EPA-HQ-OW-2009-0297-0650
EPA Comment ID: 28824
EPA Comment Code: 6140

Comment: Document ID No. EPA-HQ-OW-2009-0297

Additional NDEP Comments to "Drinking Water: Perchlorate Supplemental Request for Comments" noticed by the USEPA in the August 19, 2009 Federal Register.

These additional comments focus on: (1) the lack of a demonstrative environmental or public health benefit being realized when an MCL is applied to existing well-managed remediation sysytems in the Las Vegas Valley if a low standard is developed that does not consider all of the recent epidemiological literature; and (2) analytical challanges associated with accurately measuring perchlorate in water with elevated EC.

October 8, 2009

U.S. Environmental Protection Agency Mailcode 2822T 1200 Pennsylvania Ave., NW. Washington, DC 20460

Subject: Docket ID No. EPA-HQ-OW-0297

Reference: Drinking Water: Perchlorate Supplemental Request for Comments (Federal Register / Vol. 74, No. 159 / Wednesday, August 19, 2009 / Notices

The Nevada Division of Environmental Protection (NDEP) submits these additional comments in response to the referenced "Supplemental Request for Comments" noticed by the U.S. Environmental Protection Agency (EPA) in the August 19, 2009 Federal Register; Docket ID No. EPA-HQ-OW-2009-0297. These comments are submitted in addition to comments previously provided by the NDEP dated September 16, 2009. The comments are provided within the extended comment period and are designed to assist the EPA in their efforts in evaluating whether there is a meaningful opportunity for human health risk reduction of perchlorate to persons served by public water systems through promulgating a national primary drinking water rule for perchlorate.

The NDEP understands that in order to regulate a contaminant in drinking water [i.e., develop a maximum contaminant level (MCL)], EPA must determine that the contaminant meets the following three criteria:

1) The contaminant may have an adverse effect on human health;

2) The contaminant is known to occur (or there is a substantial likelihood that the contaminant will occur) in public water systems, with a frequency and at levels of public health concern; and

3) Regulation of such a contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

These additional comments focus on two primary elements:

* The lack of a demonstrative environmental or public health benefit being realized when a drinking water standard (maximum contaminant level [MCL]) is applied to permitted waste water discharges from existing well-managed remediation systems in the Las Vegas Valley if a low standard is developed that does not consider all of the recent epidemiological literature; and

* analytical challenges associated with accurately measuring perchlorate in water with elevated electrical conductivity (EC).

Lack of Benefit Realized and Difficulties Applying a Very low MCL:

MCLs are used by States, Territory's, and the Federal government to determine when an action may be required (action level) as well as when remediation may cease (remediation standard). Additionally, many regulatory agencies (including the NDEP) use MCLs, when they are available, for water quality criteria applicable to water quality permits. Two principal permit programs overseen by the NDEP in the State of Nevada are the National Primary Discharge Elimination System (NPDES) program and the Underground Injection Control (UIC) program. Permits issued by these programs not only are used to regulate the water quality of waste water discharges from various industries and governmental entities; these permits are also used to regulate the water quality of discharges from environmental remediation systems. Use of MCLs to set discharge limitations in these permitting programs where drinking water is the designated beneficial use of the receiving water is typical throughout the US.

Two significant environmental remediation projects are actively remediating perchlorate-impacted groundwater within the Las Vegas Valley (NDEP 2009). Tronox (formerly Kerr-McGee) operates a Fluidized Bed Reactor (FBR) that treats approximately 1,000 gallons per minute (gpm) with a typical influent concentration of approximately 500 milligrams per liter (mg/L) perchlorate. AMPAC operates an In-situ Bioremediation (ISB) system that treats approximately 200 to 300 gallons per minute with a typical influent concentration of 20 to 30 mg/L perchlorate. Both treatment systems additionally treat (destroy) large amounts of chlorate and nitrate due to the advantageous use of bioremediation. Bioremediation of perchlorate is nonselective; hence significant environmental and human health benefits are realized through use of these technologies (FBR and ISB) to treat large volumes of water impacted with elevated concentrations of perchlorate.

Both the Tronox and AMPAC bioremediation systems are designed to operate with more electron donor provided than is necessary to destroy all of the nitrate, chlorate, and perchlorate present within the influent water. These treatment systems are designed this way because it would be incredibly difficult to precisely meter an amount only necessary for the required mass destruction given that small changes in influent concentrations (of perchlorate, chlorate, and nitrate) occur. As such, the treatment systems are designed and the actual operations are managed in ways that the treated water typically exhibits no detectable concentration of perchlorate. Stated another way, there is no advantage to operate these remediation systems in a manner that conserves electron donor but puts the permittee (Tronox and AMPAC) at risk of a NPDES or UIC permit violation.

The practical challenge is not one of treatment system design and operation, but rather of monitoring. Significant challenges exist in identifying and quantifying perchlorate in the Tronox NPDES permitted discharge and AMPAC UIC permitted discharge at values typically less than approximately 10 ug/L and 6 ug/L, respectively. Additionally, the actual environmental benefit that could be perceived to be present if the permit discharge values were lowered significantly is in the

range of less than 1/2 pound per day mass loading to the receiving waters. The down side associated with placing a significantly lower standard on the referenced permits is that the two treatment systems would be precariously positioned for permit exceedance. It makes little sense to the NDEP to effectively establish discharge permit conditions that increase potential for noncompliance with two very important and very successful perchlorate treatment systems and at the same time provide no measureable environmental benefit or public health risk reduction.

Analytical Challenges:

Most perchlorate remediation that occurs throughout the United States involves significantly lower concentrations of perchlorate particularly when higher amounts of water are treated. Additionally, the baseline water quality applicable to those remediation projects is much different on those projects than for projects within the and Mojave Desert region of the southwestern United States including projects within the Las Vegas Valley. Total dissolved solids (TDS) concentrations of shallow groundwater within the Las Vegas Valley typically exceed 1,000 mg/L and often can be measured between 3,000 and 10,000 mg/L. Electrical conductivity (EC) measurements (specific conductance) often are used in lieu of TDS measurements to permit rapid, cost-effective analysis of water quality when monitoring ground water, surface water, and NPDES and UIC permitted discharges. Although EC and TDS measurements are not identical, the two are well correlated.

It is important to note that the treated water discharged from the Tronox FBR remediation system typically measures in the range of 10,000 mg/L. Similarly, it is helpful to know that the donor-amended water injected via a UIC permit by AMPAC to allow for ISB of perchlorate typically measures in the range of 3,000 to 4,500 mg/L TDS. The analytical method routinely used to quantify perchlorate in water is EPA Method 314.0 or 314.1. Both of these Ion Chromatography (IC) based methods do not provide reliable results when the water samples being tested are in the range (or exceed) approximately 7,000 us/cm (reference Table 1 and the related analytical summaries in Attachment A). Additionally, these methods are presumptive methods in that they do not provide a definitive determination that the detected analyte is perchlorate as can be seen in Table 1. The influent water to the above referenced treatment systems additionally contain a number of other analytes that can co-elute or otherwise compromise the detection and quantification of perchlorate. It is for these reasons that:

* Other methods have been developed for use particularly with saline samples;

* Mass spectrometry (MS) is used as the detector in more robust analytical methods that are preferred by many knowledgeable chemists and other professionals working with perchlorate identification, quantification, and remediation as these advanced methods provide superior results; and

* It is very difficult to identify and quantitate perchlorate to very low concentrations (generally less than between 6 and 10 ug/L) in water that exhibits elevated TDS and/or other confounding analytes.

In summary, the NDEP recommends EPA conduct a thoughtful review of all of the data and literature at this time. EPA should consider the side-effects and unnecessary costs external to the Safe Drinking Water Program (SDWA) that are involved with using the proposed methodologies to set an MCL at a level that is not readily attainable nationally using available analytical methods and

readily available equipment. Alternatively, EPA should demonstrate additional measureable environmental or public health benefit that would justify these additional external costs. The selection of appropriate analytical methods for use in different applications (drinking water, waste water, treated water from remediation systems) is crucial to enable the collection of useable data. Additionally, the application, of a scientifically based defensible regulatory standard (Health Advisory, MCL, or other standard) throughout the perchlorate remediation and monitoring process is a critical component to successful remediation and monitoring of perchlorate in environmental media.

We trust the EPA will thoughtfully consider our comments and those submitted by other entities during its current evaluation.

Sincerely, Tom Porta, Deputy Administrator Nevada Division of Environmental Protection

Tp/tjc cc Jennifer Carr, P.E., CEM, Chief, Bureau of Safe Drinking Water, Nevada Division of Environmental Protection, 901 S. Stewart Street, Suite 4001, Carson City, NV 89701-5249 Darrel Osterhoudt, Regulatory Affairs Manager, Association of State Drinking Water Administrators, 1401 Wilson Blvd., Suite 1225, Arlington, VA 22209 Kay Brothers, Deputy General Manager, SNWA Engineering/Ops, Southern Nevada Water Authority, 100 City Parkway, Suite 700, Las Vegas, NV 89106 Dr. Mic Stewart, Manager, Water Quality Section, Metropolitan Water District of Southern California, 700 North Alameda Street, Los Angeles, CA 90012 Marie Pearthree, Assistant General Manager, Central Arizona Water Conservation District, PO Box 43020, Phoenix, AZ 85080-3020 Brenda Pohlmann, Environmental Programs Manager, City of Henderson, PO Box 95050, Henderson, NV 89009 Susan Crowley, Tronox, LLC, PO Box 55, Henderson, NV 89009 Jeff Gibson, AMPAC, 3883Howard Hughes Parkway, Suite 70, Las Vegas, Nevada 89109

Table 1: Comparison of Analytical Methods used for Measuring Perchlorate in Aqueous Samples [see PDF docket ID EPA-HQ-OW-2009-0297-0650]

Attachment A [see PDF Docket ID EPA-HQ-OW-2009-0297-0650]

References:

Federal Register, 2008, Final Update IV, SW-846, Volume 73, Number 2; (wais.access.gpo.gov) [DOC ID:fr03ja08-36]

Interstate Technical Regulatory Council, 2005, Perchlorate: Overview of Issues, Status, and Remedial Actions, ITRC Document, September 2005

Magnuson, Matthew L., Urbansky, Edward T., and Kelty, Catherine A., 2000, Determination of Perchlorate at Trace Levels in Drinking Water by Jon-Pair Extraction with Electrospray Ionization Mass Spectrometry, Analytical Chemistry, Vol. 72 No. 1, January 1, 2000

Nevada Division of Environmental Protection (NDEP), 2009, Response to Supplemental Request for Comments, noticed by the US Environmental Protection Agency in the August 19, 2009 Federal Register; Docket ID No. EPA-HQ- OW-2009-0297

Sellers, Kathleen, Aslop, William, Clough, Stephen, Hoyt, Marilyn, Pugh, Barbara, Robb, Joseph and Weeks, Katherine, 2007, Perchlorate: Environmental Problems and Solutions; CRC Press, Boca Raton, FL. Chapter 3, pgs. 43 to 63

Shen-yi Yang, 2007, SW 846 Methods for The Analysis of Perchlorate in Various Environmental Media, Power Point Presentation, USEPA Office of Solid Waste.

USEPA, 1999, Method 314.0, Determination of Perchlorate in Drinking Water Using Ion Chromatography, Rev. 1.0. Available at www.epa.gov/safewater/methods/source.html

USEPA, 2005a: Method 314.1, Determination of Perchlorate in Drinking Water Using Nine Column Concentration/Matrix Elimination Ion Chromatography with Suppressed Conductivity Detection, Rev. 1.0, Available at www.epa.gov/safewater/methods/source.html. EPA Document No. EPA 815-R-05-009.

USEPA, 2005b, Method 331.0, Determination of Perchlorate in Drinking Water by Liquid chromatography Electrospray Ionization Mass Spectrometry, Rec. 1.0. Available at www.epa.gov/safewater/methods/source.html. EPA Document No. 815- R-05-007.

USEPA, 2005c, Method 332.0, Determination of Perchlorate in Drinking Water by Ion Chromatography with Suppressed Conductivity and Electrospray Ionization Mass Spectrometry. Available at www.epa.gov/safewater/methods/souree.html. EPA Document No. EPA/600/R-05/049.

USEPA, 2007, Method 6850, Perchlorate in Water, Soil and Solid Wastes Using High Performance Liquid Chromatography/Electrospray Ionization/Mass Spectrometry (HPLC/ESI/MS or HPLC/ESI/MS/MS). Available at http://www.epa.gov/SW-846

USEPA, 2008, Method 314.2, Determination of Perchlorate in Drinking Water Using Tow-Dimensional Ion Chromatography with Suppressed Conductivity Detection, Ver. 1.0. Available at www.epa.gov/safewater/methods/source.html. EPA Document No. 815-B-08-001

Response: EPA will continue to evaluate the available science related to perchlorate, the feasibility of analytical methods, and the costs and benefits of regulation, as part of its decision making process to set an MCL for perchlorate. Please note, however, that SDWA excludes from EPA's cost/benefit analysis the consideration of costs and benefits resulting from compliance with other regulatory programs. SDWA Section 1412(b)(3)(C). Please also see response to comment ID 28813 under comment code 6140.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0415
EPA Comment ID: 28855
EPA Comment Code: 6140

Comment: Consideration of Studies Published since EPA adopted the NAS RfD for perchlorate

In addition to the noted epidemiological, exposure assessment, and occurrence studies, AWWA would like to direct the Agency's attention to other references that should bear on the decision making process following this comment period.

- AWWA and Water Research Foundation. 2009. Hypochlorite - An Assessment of Factors That Influence the Formation of Perchlorate and Other Contaminants.

Considering that perchlorate has been under review for Federal regulation and is currently regulated in California and Massachusetts (proposed in New Jersey), this study was commissioned to quantify potential perchlorate contributions from hypochlorite sources. Sodium hypochlorite is a commonly used form of chlorine in drinking water and water reuse applications for its ability to disinfect and maintain a residual level of disinfectant throughout the distribution system. Approximately 1/3 of all drinking water treatment plants (DWTPs) in the United States use bulk hypochlorite for disinfection. [FN21: AWWA Disinfection Committee. 2008. Committee Report: Disinfection Survey Part 2 - Alternatives, experience and future plans. Journal AWWA. 100:11.] Though the majority of liquid hypochlorite use is in the form of bulk hypochlorite delivered from regional manufacturers and/or distributors, and some use on-site hypochlorite generators (OSG).

The data set for this study was limited to 12 OSG sites, 6 bulk hypochlorite sites, and 1 calcium hypochlorite site. This sample set suggested no difference between bulk sodium hypochlorite solutions, OSG solutions, and calcium hypochlorite solutions with respect to chlorate and perchlorate ion concentration, with the exception being bromate formation. The analysis did demonstrate the potential to exceed some existing state standards and HRLs proposed by the Agency. Therefore, as more pressure is placed on utilities using gaseous chlorine to move towards alternative disinfection practices for security related reasons, the sector requires more detailed information to fully characterize potential differences (in terms of contaminant formation/dosing) between the available options to avoid unintended future water quality consequences and proper consideration of the risk- risk tradeoffs.

- Russell, C., Roberson, A., Chowdhury, Z., and M. McGuire. 2009. National Cost Implications of a Perchlorate Regulation. Journal AWWA. 101:3:54.

Recognizing a lack of available information on projected national costs associated with perchlorate treatment, a study was conducted to estimate the national cost implications of setting a federal maximum contaminant level (MCL) for perchlorate at different levels between 4 and 24 ug/L. At the most stringent potential MCL evaluated (4 ug/L), the national compliance cost was estimated to be between $76 and $140 million per year at a 3% discount rate. The relatively low national compliance cost for perchlorate reflects the small number of public water systems (PWSs) expected to be affected (3.4% at a perchlorate MCL of 4 ug/L based on 90th percentile perchlorate concentrations). However, the cost impacts to an individual system installing perchlorate treatment would likely be significant. With operations and maintenance (O&M) costs for perchlorate treatment over a 20-year period comparable to the capital costs for construction and with these O&M costs continuing in perpetuity, ratepayers could face a significant increase.

Response: As the NPDWR is developed, economic feasibility will be evaluated in support of identifying an MCL. EPA will consider the best available, peer reviewed literature on the full range of issues embodied in an NPDWR, including risk-risk tradeoffs.

Commenter Name: Danielle Blacet
Commenter Organization: Association of California Water Agencies
EPA Document ID: EPA-HQ-OW-2009-0297-0208
EPA Comment ID: 28920
EPA Comment Code: 6140

Comment: Since approximately 1/3 of all drinking water treatment plants (DWTPs) in the United States use bulk hypochlorite for disinfection, hypochlorite should be considered as a source of perchlorate contamination in finished drinking water.[FN2: AWWA and Water Research Foundation. 2009. Hypochlorite - An Assessment of Factors That Influence the Formation of Perchlorate and Other Contaminants.] Sodium hypochlorite is a commonly used form of chlorine in drinking water. Because the AWWA-WRF analysis demonstrated the potential to exceed some existing state standards and HRLs proposed by USEPA, the results of this study should be reviewed when finalizing the regulatory determination, and also included in the discussion regarding existing and future drinking water disinfection practices.

Response: EPA is aware of this study and agrees that it should be considered in developing the NPDWR.

Commenter Name:
Commenter Organization: Intertox, Inc.
EPA Document ID: EPA-HQ-OW-2009-0297-0662
EPA Comment ID: 28938
EPA Comment Code: 6140

Comment: APPENDIX B

INITIAL REVIEW OF HOPONICK ET AL., 2009

Initial Review of: Hoponick JR, Melillo PR, Visser NT and Henshel DS. 2009. "Examining the Correlation between Perchlorate Concentrations in California Drinking Water and Low Birth Weight Percentage Using Population-Scale Regression Analysis," obtained from C. Matthews, Contractor, US EPA, Office of Environmental Information, EPA Docket Center, EPA Docket OW-2009-0297-0492, received via email on September 30, 2009.[FN1: http://www.regulations.govisearch/Regs/contentStreamer?objectId= 0900006480a27182&disposition=attachment&contentType=xml]

This document (Hoponick et al., 2009) appears to be a manuscript that has been submitted for publication. The study is an ecological epidemiological study, and is short in length. The authors evaluate the association between the mean perchlorate concentration measured in groundwater wells in 13 counties in California (measured between 1997 and 2004), and the percent of neonatal births with low birth weight (LBW), coded by zip code from 1993 to 2002. Zip code data sets for percent of births with LBW for each year were "averaged to the county level by averaging all data within each county." Based on this evaluation, the authors conclude that "log perchlorate data are significantly correlated with LBW for all years" and that "the increase is relatively linear from the lowest detectable perchlorate levels (3.3 ppb) to about 10 ppb, where the response appears to saturate." They further conclude, "Log perchlorate data also significantly positively correlates with TSH level for 1998, the only year for which TSH data was available."

An initial analysis of the manuscript was conducted using information derived from the manuscript. The source of data and an analysis of the methods and conclusions is provided below. Comments are divided into the following categories: data related to perchlorate concentrations in drinking water, data related to LBW, data related to neonatal TSH, and discussion of confounding factors.

EPA should review the scientific basis of this manuscript to assure itself that the data are reliable. Upon request, additional information can be provided. What might be useful is to review a recently published paper which reports no effect on birth weight, head circumference, and body length associated with perchlorate exposure (Blount et al., 2009). Briefly, the following is noted regarding the manuscript.

Perchlorate Concentrations in Drinking Water

Hoponick et al. (2009) conducted statistical analyses using the mean concentrations of perchlorate in drinking water,[FN2: The paper alternatively calls the water source either "groundwater wells" or "drinking water wells."] collected between 1997 and September 9, 2004, and averaged across each of 13 counties. The authors present mean concentrations for any California county that "contained two or more perchlorate detections from at least one drinking water source since 1997." Data were obtained from the California Department of Health Services website: http://www.cdph.ca.govicertlic/drinkingwater/Pages/Perchloratehistory.aspx. A downloadable MS Excel file of the data is here: http://www.cdph.ca.gov/certlic/drinkingwater/Documents/Perchlorate/Perchloratefo rwebearlyfindings.XLS.

Some observations about these data are as follows:

* The CDHS website only provides downloadable data for detects of perchlorate in water only. It is not clear from the manuscript whether the analysis considered nondetects in the calculation of mean perchlorate concentrations.

* Neither the CDHS website nor the manuscript indicate the analytical method that was used to measure perchlorate during this time. For example, a change in analytical method could impact the concentration data.

* The manuscript does not indicate the range of concentrations detected in the wells, the number and percentage of wells or water systems in which perchlorate was detected in each county, or how frequently perchlorate was detected in specific wells.

* The data obtained from CDHS shows that many wells were sampled repeatedly. However, the manuscript does not indicate how multiple detections at the same location were considered in the calculation of the county average.

* The manuscript does not indicate the extent to which sampled wells contribute to drinking water for the public in a given county, or whether water from wells was treated prior to distribution (but after sampling).

* Some of sample dates in the CDHS database cannot be discerned because they appear to be miscoded.

* The manuscript does not indicate how the timing of sample collection was assumed to relate to the association with LBW data.

* It appears that some average concentrations reported in the manuscript include data from wells designated in the CDHS database as "inactive" or "destroyed," and therefore would not contribute to drinking water that is distributed to the public. It is not clear how inclusion of these data is assumed to provide reliable measures of exposure.

Percent of Neonatal Births with Low Birth Weight (LBW)

Hoponick et al. (2009) report that data on neonatal birth weights were obtained from the California Department of Public Health (CDPH) for the years 1993 to 2002. The authors define "low birth weight" as a birth weight less than 2,500 grams (5.5 lbs.). The link provided in the paper redirects to here: http://ww2.cdph.ca.gov/programs/deodc/Pages/default.aspx. Annual data by zip code for the years 1993 to 2002 are available.[FN3: 1993:
http://ww2.cdph.ca.gov/data/statistics/Documents/birthzip1993.xls 1994:
http://ww2.cdph.ca.gov/data/statistics/Documents/birthzip1994.xls 1995:
http://ww2.cdph.ca.gov/data/statistics/Documents/birthzip1995.xls 1996:
http://ww2.cdph.ca.gov/data/statistics/Documents/birthzip1996.xls 1997:
http://ww2.cdph.ca.gov/data/statistics/Documents/birthzip1997.xls 1998:
http://ww2.cdph.ca.gov/data/statistics/Documents/birthzip1998.xls 1999:
http://ww2.cdph.ca.gov/data/statistics/Documents/birthzip1999.xls 2000:
http://ww2.cdph.ca.gov/data/statistics/Documents/birthzip2000.xls 2001:
http://wv2.cdph.ca.gov/data/statistics/Documents/birthzip2001.xls 2002:
http://ww2.cdph.ca.gov/data/statistics/Documents/birthzip2002.xls]

Some initial observations of these data are as follows:

* %LBW is lowest in 1996 for six of 13 counties and highest in 2002 for eight of 13 counties. The manuscript does not discuss these differences, or how they might relate to perchlorate exposure. For example, might there have been a change in the measurement or reporting method for birth weight?

* Sacramento County has 135 zip codes, but in 2002 (for example) the CDPH data only includes birth weight data for 49 zip codes. Further, the CDHS data includes only 34 water samples for perchlorate (from a total of 14 locations in five systems), after exclusion of data from inactive or destroyed wells. It is not clear how from the manuscript how data from these wells was extrapolated to assumed exposure across the county, or to specific zip codes, and how birth weight data for missing zip codes was considered. It appears that all individuals in the county were assumed to be exposed to the average perchlorate concentration computed from the available samples, and that the county average %LBW was based on the 49 zip codes for which data were available.

Neonatal TSH Data

The manuscript remarks "TSH data was obtained by contacting the CDHS directly, and 1998 was the only year CDHS provided." We were not able to find the data in the manuscript to support this statement.

Confounding Factors

The manuscript states, "The confounding factors data from 2003 was obtained from the California Interview Survey (CHIS) Database, which is operated by the University of California Los Angeles Center for Health Policy Research, in cooperation with CDHS and the Public Health Institute." The CHIS database is available (http://www.chis.ucla.edu/getdata.html). The only confounding variables reportedly considered by the authors were race and percentage of uninsured individuals. However, the literature on low birth weight is extensive and many other factors are known to influence birth weight including maternal health status, maternal age, smoking, alcohol/ drug use, prenatal care, maternal education level, and other socio-economic factors (Bailey and Byrom, 2007; Nobile et al., 2007). It appears that these factors were not evaluated.

References

Bailey BA, Byrom AR. 2007. Factors predicting birth weight in a low-risk sample: the role of modifiable pregnancy health behaviors. Matern Child Health J11(2):173-9.

Blount BC, Rich DQ, Valentin-Blasini L, Lashley S, Ananth CV, Murphy E, Smulian JC, Spain BJ, Barr DB, Ledoux T, Hore P, Robson M. 2009. Perinatal Exposure to Perchlorate, Thiocyanate, and Nitrate in New Jersey Mothers and Newborns. Environ Sci Technol [Epub ahead of print].

Nobile CG, Raffaele G, Altomare C, Pavia M. 2007. Influence of maternal and social factors as predictors of low birth weight in Italy. MC Public Health 7:192.

Response: EPA will use the best available, peer reviewed science in preparing the NPDWR for perchlorate.

Commenter Name: Tom Porta
Commenter Organization: Nevada Division of Environmental Protection (NDEP)
EPA Document ID: EPA-HQ-OW-2009-0297-0638
EPA Comment ID: 29100
EPA Comment Code: 6140

Comment: The August 19, 2009 Federal Register Notice indicates that EPA is considering using monitoring data from the State of Massachusetts to help characterize the distribution of very low perchlorate concentrations occurrences. Evidence needs to be provided to support the use of Massachusetts (or other discrete) monitoring data for the purpose indicated. EPA has not demonstrated how these data sets are representative of the nation as a whole. Model calibration should be conducted with robust data that are representative of the nation's water supply systems to make informed decisions regarding a national primary drinking water standard. Consequently, the NDEP recommends collection of new data for perchlorate in public water systems, coupled with the use of more sensitive analytical methods with greater specificity (EPA Method 331 or EPA Method 332). Newer, more sensitive analytical methods will provide more reliable and robust data, rather than trying to estimate values (< 4 ug/L) that are not part of the existing, outdated occurrence

data generated using a less sensitive analytical method (EPA Method 314). The referenced more sensitive methods have several method refinements (different column packing material, longer columns, mass spectrometry detectors) that lead to fewer false positives or false negatives and permit perchlorate analysis with reporting limits (detection limits) at or below 1 ug/L. These newer data are more robust and capable of multiple uses without limitations inherent in estimated data.

Response: EPA agrees that newer analytical methods are more sensitive. Information from a variety of sources will be used in developing the NPDWR. EPA is required to use the best available, peer reviewed science in its deliberations. The strengths and limitations will be considered as those deliberations proceed.

EPA Comment Code: 6200 Comments related to EPA's health advisory

Individual Comments
Commenter Name: Kathy M. Kinsey
Commenter Organization: Maryland Department of the Environment
EPA Document ID: EPA-HQ-OW-2008-0692-1421
EPA Comment ID: 20428
EPA Comment Code: 6200

Comment: A Health Advisory for Perchlorate Will Undermine Cleanup Efforts

The establishment of a uniform federal standard is especially important to eliminate potentially conflicting state standards, particularly in cases of cross-boundary contamination. Merely publishing a health advisory for perchlorate, as EPA has proposed, will undermine expeditious cleanup of contaminated sites and regulation of discharges to interstate surface waters used to supply drinking water. A health advisory is not binding or enforceable, and does not ensure a uniform nationwide standard. Rather, it leads to a patchwork of different state standards and in the absence of a state standard, cleanup standards for individual sites that must be established through negotiation on a case-by-case basis.

Response: See response to comment ID 28479 under comment code 6200.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association
EPA Document ID: EPA-HQ-OW-2008-0692-1424
EPA Comment ID: 20441
EPA Comment Code: 6200

Comment: Health Advisory

AWWA supports the EPA decision to issue a Health Advisory for perchlorate at the timeof the final determination. Health advisories provide important technical guidance to Federal agencies, State governments, and other public health officials on health effects, analytical methodologies, and treatment technologies. EPA should, in parallel, issue are vision of the "Assessment Guidance for Perchlorate" released by the Office of Solid Waste and Emergency Response (OSWER) on January 26, 2006, which defines the remediation goal for perchlorate in accordance with National Oil and Hazardous Substances Contingency Plan (National Contingency Plan, NCP), 40 CFR Part 300. In addition, any potential remediation action should consider all applicable or relevantand appropriate (ARAR) requirements under federal environmental or state environmental or facility siting laws.

Response: See response to comment ID 28479 under comment code 6200. A Health Advisory will no longer be needed.

Commenter Name: Ed Thomas
Commenter Organization: National Rural Water Association
EPA Document ID: EPA-HQ-OW-2008-0692-1669

EPA Comment ID: 20618
EPA Comment Code: 6200

Comment: Based on the occurrence, health risk, and related findings presented in the Agency's analysis we also believe that a health advisory is appropriate. It is evident that perchlorate is a problem in specific targeted areas. A health advisory will provide the acceptable levels that are safe for local communities with contaminated source water.

Response: See response to comment ID 28479 under comment code 6200. A Health Advisory will not be needed.

Commenter Name: Paul J., P.E. Ponturo
Commenter Organization: Long Island Water Conference
EPA Document ID: EPA-HQ-OW-2008-0692-1260
EPA Comment ID: 20624
EPA Comment Code: 6200

Comment: In the preliminary determination, EPA has indicated that States that are known to have perchlorate concentrations at or above the HRL should develop their own regulations, and has stated its intent to provide the States with a Health Advisory Level at the same time it finalizes this determination. We wish to state for the record that we will ask the State of New York for an enforceable MCL to be adopted. The Long Island Water Conference's member suppliers are fully supportive of science-driven regulations that are most protective of public health, and to that end have in some cases voluntarily installed treatment or modified operational practices to reduce the use of wells containing perchlorate.

Response: See response to comment ID 28479 under comment code 6200.

Commenter Name: James Taft
Commenter Organization: Association of State Drinking Water Agencies
EPA Document ID: EPA-HQ-OW-2008-0692-1527
EPA Comment ID: 20635
EPA Comment Code: 6200

Comment: A Health Advisory is step one - If the Agency is not going to develop a full national regulation, it needs to provide adequate support for those entities (water systems and states) that are going to respond at the local level. In the Federal Register notice, EPA committed to publishing a health advisory for perchlorate at the time of the final determination in order to provide information regarding potential health risks from perchlorate-contaminated drinking water. States fully support this action and recommend that the Agency provide the health advisory as soon as possible. While this may be enough to help states and water systems determine when perchlorate is approaching levels of health concern, it will not provide the level of technical support necessary for states and water systems to address perchlorate contamination problems.

Response: See response to comment ID 28479 under comment code 6200.

Commenter Name: Mic Stewart
Commenter Organization: Metropolitan Water District of Southern California

EPA Document ID: EPA-HQ-OW-2008-0692-1784
EPA Comment ID: 20663
EPA Comment Code: 6200

Comment: * Public Health Advisory for Perchlorate - Metropolitan recommends that any public health advisory for perchlorate in drinking water issued by the EPA include language that provides the greatest possible public health protection, particularly for pregnant women and other sensitive sub-populations (e.g., infants and children).

Response: See response to comment ID 28479 under comment code 6200. A Health Advisory will not be needed.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1855
EPA Comment ID: 21102
EPA Comment Code: 6200

Comment: IX. EPA Should Make Conforming Changes to its Regulation and Policies Consistent with this Determination

At the same time of its final determination, EPA should maintain its March 2006 guidance for use by EPA regions and states, but update it with the new Health Advisory, if the decision is made to set one. The RfD is a conservative safe dose as has been noted throughout our comments. The current guidance allows state and local officials to factor in site-specific considerations and populations as opposed to making local decisions guidance data based upon nationally representative exposure data.

Issuing a health advisory and revised guidance at the same time as the agency issues a final determination provides a strong clear message from EPA headquarters to EPA regions as well as state and local public health officials on the final federal policy related to perchlorate. It brings to close any uncertainty at the federal level on the issue, thereby providing state and local officials with regulatory certainty and allowing them to move forward in addressing site-specific contamination.

Response: See response to comment ID 28479 under comment code 6200. A Health Advisory will not be needed.

Commenter Name: Ed Thomas
Commenter Organization: National Rural Water Association (NRWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0521
EPA Comment ID: 28475
EPA Comment Code: 6200

Comment: Based on the occurrence, health risk, and related findings presented in the Agency's analysis we also believe that a health advisory is appropriate. It is evident that perchlorate is a problem in specific targeted areas. A health advisory will provide the acceptable levels that are safe for local communities with contaminated source water.

Response: See response to comment ID 28479 under comment code 6200.

Commenter Name: Mark S. Mayer
Commenter Organization: South Dakota Department of Environment & Natural Resources (DENR)
EPA Document ID: EPA-HQ-OW-2009-0297-0467
EPA Comment ID: 28479
EPA Comment Code: 6200

Comment: - Where Perchlorate is a problem, it is important that EPA provide resources to those states to appropriately and consistently respond. The first step should be for EPA to establish a health advisory that can be used to identify potential problems at the local level.

Response: EPA has determined the need to regulate perchlorate and will develop a NPDWR. As a result, a health advisory will not be necessary.

Commenter Name: James D. Taft
Commenter Organization: Association of State Drinking Water Administrators
EPA Document ID: EPA-HQ-OW-2009-0297-0525
EPA Comment ID: 28505
EPA Comment Code: 6200

Comment: A Health Advisory is step one - If the Agency is not going to develop a full national regulation, it needs to provide adequate support for those entities (water systems and states) that are going to respond at the local level. In the October 2008 Federal Register notice, EPA committed to publishing a Health Advisory for perchlorate at the time of the final determination in order to provide information regarding potential health risks from perchlorate- contaminated drinking water. States fully support this action and recommend that the Agency finalize the interim January 2009 health advisory as soon as possible. ASDWA also recommends that EPA prepare educational materials to help states and water systems use the Health Advisory to educate the public about perchlorate in the systems where it is detected.

Thank you for your consideration of these comments. Please contact me at 703-812-9507 or jtaft@asdwa.org if we can provide additional information or if any clarification of these comments is needed.

Sincerely, James D. Taft Executive Director

Response: See response to comment ID 28479 under comment code 6200.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0494
EPA Comment ID: 28832
EPA Comment Code: 6200

Comment: In addition, if EPA chooses to update its health advisory, AMWA recommends that the agency take care to explain the difference between perchlorate and other chemical compounds. Perchlorate is an endocrine disruptor and in the words of one peer reviewer,

"However, as noted above, what is still needed at the beginning of the document is a brief overview of the toxicokinetics of perchlorate, iodine as an essential element for the synthesis of thyroid hormones, why thyroid hormone sufficiency is important, what homeostasis is - perchlorate affects a self-regulating system which has evolved numerous feedback mechanisms to compensate for deficiency induced by inadequate intake, iodine uptake inhibition, illness and that within the homeostatic range, which is robust in humans, this system is successful. [The same would be true for excess.] In other words, the biological impacts of perchlorate are very different from those for chemical compounds which have direct target organ toxicity and/or do not directly affect the availability of an essential element for which homeostasis occurs." (EPA, 2008. Comment- Response Summary Report. Peer Review of Drinking Water Health Advisory for Perchlorate, page 7).

Response: EPA agrees that this suggested information should be incorporated into support documentation for the impending NPDWR.

EPA Comment Code: 6210 Need for EPA to provide additional support to States and water systems

Individual Comments
Commenter Name: Paul J., P.E. Ponturo
Commenter Organization: Long Island Water Conference
EPA Document ID: EPA-HQ-OW-2008-0692-1260
EPA Comment ID: 20625
EPA Comment Code: 6210

Comment: However we wish to point out that those States that need to develop their own standards, potentially as many as 26 according to the preliminary determination, will need to make other complex decisions beyond establishing an MCL. EPA knows the importance of a fully-formed regulation that is legally defendable. To that end decisions will need to be made as to acceptable analytical methodologies, best available treatment technology and treatment residuals disposal, minimum analytical frequencies, and perchlorate occurrence processes. It should also be recognized that companion regulations will need to be developed to identify and restrict industrial applications and storage of chemicals containing perchlorate. Unmeasured perchlorate may exist in products in common use, yet the users may be unaware of a potential concern. As previously stated, many perchlorate detections do not trace to known sources.

Therefore we do wish to state our concern that states may lack the resources to develop a robust regulatory response to their individual perchlorate issues. We would respectfully request that EPA's guidance to the states should also incorporate a Federal resource commitment to the other aspects of the regulatory problem that the states will have to face. EPA should also continue to be a clearing house of information on perchlorate and commit research dollars to encourage the development of economically viable treatment alternatives, and to better understand perchlorate occurrence.

The Conference appreciates your consideration of these comments and looks forward to seeing the continued development of this important regulation.

Very truly yours, Kenneth S. Claus Chairman, Long Island Water Conference

Response: See the response to comment code 6120. EPA acknowledges commenter's concern about decisions that will need to be made as to acceptable analytical methodologies, best available treatment technology and treatment residuals disposal, minimum analytical frequencies, and perchlorate occurrence processes. These issues are factors that EPA will consider when developing a NPDWR for perchlorate. Upon promulgating a NPDWR, EPA will provide States and public water systems with information in regards to perchlorate treatment techniques. EPA acknowledges commenter's statement "…It should also be recognized that companion regulations will need to be developed to identify and restrict industrial applications and storage of chemicals containing perchlorate." However this subject matter pertains to EPA's RCRA regulations and falls outside of the scope of this regulatory action.

Pursuant to SDWA section 1412(b)(4)(E), 42 USC 300g-1(b)(4)(E), when EPA publishes a NPDWR establishing an MCL, the Administrator must list technologies, treatment techniques, and other means that the Administrator finds feasible for meeting the MCL, and:

The Administrator shall include in the list any technology, treatment technique, or other means that is affordable, as determined by the Administrator in consultation with the States, for small public water systems serving--

(I) a population of 10,000 or fewer but more than 3,300;

(II) a population of 3,300 or fewer but more than 500; and

(III) a population of 500 or fewer but more than 25;

and that achieves compliance with the maximum contaminant level or treatment technique, including packaged or modular systems and point-of-entry or point-of-use treatment units.

Commenter Name: James Taft
Commenter Organization: Association of State Drinking Water Agencies
EPA Document ID: EPA-HQ-OW-2008-0692-1527
EPA Comment ID: 20636
EPA Comment Code: 6210

Comment: Provide additional guidance to support states and water systems - In addition to the health effects, systems will need to know what treatments are effective for various types of source water and levels of perchlorate. Systems will also need information to help them evaluate non-treatment alternatives to perchlorate control (if available). ASDWA would be willing to work with EPA and other partners to determine what supporting materials should be developed.

Thank you for your consideration of these comments. We feel that perchlorate is somewhat of a special case due to its high profile and potential for causing adverse health effects and therefore deserves something beyond just a health advisory to support state drinking water programs. We hope the Agency will be willing to take these additional steps and we are ready to help develop a reasonable plan. Please contact me at 703-812-9507 or jtaft@asdwa.org if we can provide additional information or if any clarification of these comments is needed.

Sincerely, James D. Taft Executive Director

Response: EPA agrees and has decided to regulate perchlorate in drinking water. See response to comment code 6120. Pursuant to statutory requirements, EPA intends to publish and seek public comment on technology, treatment techniques, and other means which the Administrator finds to be feasible for purposes of meeting the proposed maximum contaminant level. The proposed regulation will also include an assessment of alternative treatment techniques that EPA is considering.

Commenter Name: Tina Carroll
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2189
EPA Comment ID: 22382
EPA Comment Code: 6210

Comment: I am deeply concerned that there known sources of perchlorate contamination in our area and the EPA has chosen to do nothing about it. All Americans deserve healthy and clean drinking water and I urge you to reverse your decision and to set a national drinking water standard for perchlorate.

Sincerely, Tina Carroll 3253 Chestnut Avenue Baltimore, MD 21211

Response: EPA has decided to regulate perchlorate in drinking water. See response to comment code 6120.

Commenter Name: Mark S. Mayer
Commenter Organization: South Dakota Department of Environment & Natural Resources (DENR)
EPA Document ID: EPA-HQ-OW-2009-0297-0467
EPA Comment ID: 28480
EPA Comment Code: 6210

Comment: - Where Perchlorate is a problem, it is also important that EPA provide technical information on effective treatment options for various source waters and levels of Perchlorate.

Response: EPA has determined that regulation of perchlorate in drinking water systems presents a meaningful opportunity to reduce health risk for persons served by public water systems. This action initiates the process to establish a national primary drinking water regulation (NPDWR) for perchlorate. EPA will provide an evaluation of feasible treatment technologies and small system compliance techniques as part of the proposed NPDWR.

Commenter Name: James D. Taft
Commenter Organization: Association of State Drinking Water Administrators
EPA Document ID: EPA-HQ-OW-2009-0297-0525
EPA Comment ID: 28504
EPA Comment Code: 6210

Comment: Additional issues - In closing, we would like to recap some of our previous comments related to the regulation of perchlorate. These are still valid points and need to be considered, regardless of what final determination is made.

Regardless of EPA's regulatory decision, states will need to act - Even if EPA does not adopt a national regulation of perchlorate, the public will likely demand a response to detections of elevated levels of perchlorate - particularly, in light of the notoriety associated with this contaminant. In states where there are detections of perchlorate at levels of concern, drinking water programs need to be able to respond appropriately so that public health can be protected. At a minimum, states will need to assist individual water systems with the specific actions needed to control perchlorate. Information is needed from EPA on risk characterization and risk management as well as treatment options and alternative control measures to support state efforts. In some cases, a state may decide that perchlorate is common enough in their source waters that they are interested in developing statewide measures, whether it is a formal monitoring program or a state specific MCL. We believe the Agency has data and expertise that can help support these actions.

Response: EPA agrees and has decided to regulate perchlorate in drinking water. See response to comment code 6120 and response to comment ID 20634 under comment code 6130.

Commenter Name: Danielle Blacet
Commenter Organization: Association of California Water Agencies
EPA Document ID: EPA-HQ-OW-2009-0297-0208
EPA Comment ID: 28921
EPA Comment Code: 6210

Comment: 3) Colorado River implications

As USEPA is aware, much of Southern California depends on a reliable water supply from the Colorado River, and our members actively participate with other Colorado River basin states to help ensure the delivery of a quantity and quality of water that will meet our environmental, urban and agricultural needs. This situation has become even more critical with the recent droughts in the Colorado River basin and California.

ACWA strongly recommends that during its science-based review and ultimate regulatory determination for perchlorate, USEPA remains cognizant of the sources and impacts from interstate perchlorate contamination to all California utilities, particularly those that rely on the Colorado River. This especially is relevant to agricultural use of Colorado River water and concentration of perchlorate in produce shipped nationwide. We would like to work with USEPA on ways to address this very important issue.

Response: EPA has determined that regulation of perchlorate in drinking water systems presents a meaningful opportunity to reduce health risk for persons served by public water systems. See response to comment code 6120. This action initiates the process to establish a national primary drinking water regulation (NPDWR) for perchlorate. In developing the proposed national primary drinking water standard, EPA will consider the degree to which perchlorate is present in public water supplies in all systems throughout the U.S. EPA intends to publish the proposed NPDWR for public comment along with health risk reduction and cost analysis, feasibility analysis and other analyses required for regulatory development under the SDWA. EPA will consider comments on the proposed NPDWR and then promulgate the final regulation.

EPA Comment Code: 6300 EPA's intention to revise guidance on clean-up levels (preliminary remediation goals)

Response to Code 6300: While EPA recognizes that perchlorate has been a contaminant of concern at a number of sites that have (or may in the future) require cleanup, it is not appropriate for the Agency to establish national primary drinking water regulations for the purpose of establishing cleanup levels at contaminated sites. Rather, the Safe Drinking Water Act specifies the criteria which compels regulation of a contaminant. EPA must determine that the contaminant meets three criteria: 1) the contaminant may have an adverse effect on human health, 2) the contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern, and 3) in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for the reduction of health risks from perchlorate for persons served by public water systems. We would note, however, that on January 8, 2009, EPA issued guidance that revised the preliminary remediation goal (PRG)[Footnote] for perchlorate in soil from 24.5 ug/L to 15/ug/L, which states that where no federal or state applicable or relevant and appropriate (ARAR) requirements exist under federal or state laws, 15 ug/L is recommended as the PRG for perchlorate when making CERCLA site-specific cleanup decisions where there is an actual or potential drinking water exposure pathway (http://www.epa.gov/fedfac/documents/perchlorate_memo_01-08-09.pdf). Depending on EPA's final decision regarding a national primary drinking water standard for perchlorate, the Agency may modify this guidance.

Footnote: PRGs are not cleanup levels, but are specific statements of desired endpoint concentrations or risk levels (55 FR 8713 (March 8, 1990)) that are conservative, default endpoint concentrations used in screening and initial development of remedial alternatives before consideration of information from the site-specific risk assessment.

Individual Comments
Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0166
EPA Comment ID: 20276
EPA Comment Code: 6300

Comment: AMWA believes that factors other than those discussed in the notice need to be considered. The contamination of water supplies by perchlorate is on-going, since perchlorate is still in use at various DoD sites, airfields and rocket manufacturing facilities. In addition, because there is no cleanup standard, perchlorate that has entered the soil and contaminated aquifers will likely spread, leading to additional impacted sites.

When a contaminant is polluting drinking water supplies and the lack of a standard is impeding pollution prevention and cleanup, then an appropriate course of action is needed. Several of the contaminants in the notice deemed appropriate for a determination not to regulate are pesticides that have not been produced or used for decades and have low and decreasing occurrence levels. Perchlorate, on the other hand, is still in use and is expected to have increasing occurrence levels as contamination migrates from soils to ground water aquifers, potentially resulting in impacts on increasing numbers of water systems - clearly a call for action.

Response: See response to comment code 6300. The Agency has determined that the three SDWA criteria for regulatory determination have been met for perchlorate. See response to commend code 6120.

Commenter Name: Diane VanDe Hei
Commenter Organization: AMWA
EPA Document ID: EPA-HQ-OW-2008-0692-1525
EPA Comment ID: 20445
EPA Comment Code: 6300

Comment: Cleanup Standards

AMWA agrees with the agency that guidance regarding perchlorate and cleanup levels under the National Oil and Hazardous Substances Contingency Plan (National Contingency Plan, NCP) should be revised downward from the present preliminary remediation goal (PRG) of 24.5 ppb. AMWA believes, however, that an appropriate PRG to protect drinking water and it users should assume that contaminated water sources would be used as drinking water. Perchlorate contaminated sites should be cleaned up to some fraction of the HRL (such as two-thirds or 10 ppb) so that any levels consumed are reliably and consistently below the HRL.

Since the recommended PRG generally is the starting point for determining appropriate site-specific cleanup levels, AMWA believes it is appropriate to start at levels that allow a margin of safety with respect to the HRL to account for the variable nature of continuing contamination and occurrence fluctuations. The level could then be adjusted up or down depending upon the site specifics. The PRG based on the HRL should not supplant more stringent state standards.

Response: See response to comment code 6300.

Commenter Name: Thomas L. Schoaf
Commenter Organization: Cities of Litchfield Park and Goodyear, AZ
EPA Document ID: EPA-HQ-OW-2008-0692-1552
EPA Comment ID: 20555
EPA Comment Code: 6300

Comment: Historical industrial operations have impacted the aquifer in the PGA North Superfund Site with TCE and perchlorate. The EPA Region 9 is currently overseeing a private party financed cleanup of the TCE impacted groundwater at the site. The remedy consists of several independent groundwater pump-and-treat systems. The treated water is either used as an irrigation supply or reinjected into the aquifer. Future remedies being considered to address the currently expanding TCE plume may entail providing the treated water for drinking water purposes. Where groundwater is being reinjected to the aquifer, EPA Region 9 is requiring the private party to treat for perchlorate as well as TCE in order to avoid aquifer degradation in areas not impacted by the plume. However, no treatment is required for water used as an irrigation supply. Since perchlorate, unlike TCE, has no established standard, EPA 9 is relying on guidance and "To Be Considered" criteria to require treatment of reinjected water at the PGA-North Superfund Site. Without the strength of a promulgated standard, we are concerned that EPA Region 9 will not be able to ensure that future remedies require perchlorate treatment. Further, guidance levels and To Be Considered criteria may

not provide EPA Region 9 the necessary authority to require that the responsible party implements an effective remedy to address the historical perchlorate contamination in the aquifer-our future water supply.

Response: See response to comment code 6300.

Commenter Name: Mic Stewart
Commenter Organization: Metropolitan Water District of Southern California
EPA Document ID: EPA-HQ-OW-2008-0692-1784
EPA Comment ID: 20664
EPA Comment Code: 6300

Comment: * Applicable or Relevant and Appropriate Requirements (ARARs) - While California has a drinking water MCL of 6 ppb for perchlorate, Metropolitan suggests that given any decision by the EPA not to regulate perchlorate, the ARARs called for in regulatory cleanup be set at the drinking water standard in states with an MCL for perchlorate. This would provide cleanup guidance for contaminated sites.

* Site specific cleanup levels - EPA states that the Health Advisory value can be used as a "to be considered value" for developing cleanup levels for perchlorate contaminated sites (i.e., Superfund). The Health Advisory value that should be stipulated in the final health advisory document will be set at a level to provide protection to the population. Sites that are potential sources of drinking water, or impact sources of drinking water, should be required to treat to a level that protects the population. A "to be considered" criteria for clean-up levels is not adequate to provide protection to the public.

Metropolitan appreciates this opportunity to provide input on the proposed regulatory determination for perchlorate and asks that EPA carefully consider these comments before publishing the final rule. Please contact me at (213) 217-5696 if you have any questions, or if I can provide additional information.

Very truly yours, Mic Stewart, PhD Manager, Water Quality Section

Response: See response to comment code 6300. The Agency has determined that the three SDWA criteria for regulatory determination have been met for perchlorate. See response to commend code 6120.

EPA Comment Code: 6310 Clean up as a solution

Individual Comments
Commenter Name: Kay Brothers
Commenter Organization: Southern Nevada Water Authority
EPA Document ID: EPA-HQ-OW-2009-0297-0648
EPA Comment ID: 28495
EPA Comment Code: 6310

Comment: October 8, 2009

Water Docket Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Avenue, NW Washington, DC 20460

SUBJECT: Comments on the Drinking Water: Percholorate Supplemental request for Comments Docket ID No. EPA-HQ-OW-2009-0297

The Southern Nevada Water Authority (Authority) submitted detailed comments, dated September 17, 2009, on the preliminary regulatory determination for perchlorate as listed in the August 19, 2009 Federal Register (74FR41883). We would like to submit the following additional comments regarding the Authority's commitment to ensure that perchlorate clean-up efforts continue along the Las Vegas Wash (Wash) upstream from Lake Mead.

As outlined in our comments previously submitted, perchlorate clean-up efforts in the Wash have significantly decreased the levels of perchlorate in Lake Mead and the lower Colorado River system. Tronox, Inc., (Tronox) owns the facility in Henderson, Nevada that produced perchlorate from 1952-2002. The site is the source of perchlorate contamination of groundwater that enters the Wash (which empties into the Colorado River). Currently, the contaminated water is intercepted at the Wash, treated in a remediation system financed by Tronox, and discharged into the Wash. The system is operated at the direction of the Nevada Division of Environmental Protection (NDEP), which estimates the current annual cost of operation at $6,000,000 with a potential remediation span of 100 years. On January 12, 2009, Tronox filed a petition for reorganization in United States Bankruptcy Court for the Southern District of New York.

The Authority, in order to actively participate in the litigation and to protect its strong interest in continued groundwater remediation and eventual elimination of the source of perchlorate contamination, hired the New York City bankruptcy firm of Kramer Levin Naftalis & Frankel. The Authority has filed a proof of claim, is examining the terms of a proposed sale of the Henderson site, and is working in concert with the Metropolitan Water District of Southern California (MET) and the Central Arizona Water Conservation District (CAP) to ensure that remediation efforts receive an adequate accounting and future funding.

To summarize, the Authority in concert with the NDEP and our partners, CAP and MET, are committed to ensuring the clean-up of perchlorate continues along the Wash. If you have any questions regarding our comments, please contact me directly at (702) 862-3707.

Sincerely, Kay Brothers Deputy General Manager Engineering and Operations

KB/df

cc: Jeffrey Kightlinger, General Manager - Metropolitan Water District of Southern California David Modeer, General Manager - Central Arizona Project

Response: No response necessary for this comment.

EPA Comment Code: 6400 EPA's decision to subject updated PBPK model to peer review during comment period (in the October 2008 FR Notice)

Response to Code 6400: EPA reviewed, modified, and applied the perchlorate PBPK models, which were originally developed by Merrill et al. (2005) for adults and Clewell et al. (2007) for other life stages, to estimate the iodide uptake inhibition in the thyroid for each life-stage (73 FR 60262). Estimated ingestion rates were then used to estimate the internal dose and resulting iodide uptake inhibition for several life stages, including susceptible populations (e.g., pregnant women and their fetuses, as well as breast-fed and bottle-fed infants).

The draft report, "Inhibition of the Sodium-Iodide Symporter by Perchlorate: An Evaluation of Lifestage Sensitivity Using Physiologically-based Pharmacokinetic (PBPK) Modeling," underwent a formal external peer review by eight experts in accordance with EPA guidance concurrently with the public comment period. Based on the external peer review comments, the models and report were revised. The final report, peer review report, and a summary of peer review comments and EPA responses are available at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=199347.

In the August 2009 notice, EPA stated that it was re-evaluating how best to incorporate the PBPK modeling analysis into its evaluation of perchlorate — if at all. The Agency sought comments on ways to use the PBPK modeling analysis to inform the regulatory determination.

After further consideration of the peer review and public comments, EPA concludes that the PBPK modeling analysis, in the context of the perchlorate regulatory determination, is useful in examining which life stages are most susceptible to the effects of perchlorate. However, because of the stated limitations, EPA has decided the model does not directly bear on the current decision regarding the need for a NPDWR for perchlorate. EPA is continuing to evaluate whether the model could be used in setting a NPDWR for perchlorate.

Individual Comments
Commenter Name: Diane VanDe Hei
Commenter Organization: AMWA
EPA Document ID: EPA-HQ-OW-2008-0692-1525
EPA Comment ID: 20443
EPA Comment Code: 6400

Comment: November 10, 2008

Water Docket U.S. Environmental Protection Agency Office of Water Docket (Mailcode 2822T) 1200 Pennsylvania Ave. NW Washington, DC 20460

RE: Drinking Water: Preliminary Regulatory Determination on Perchlorate; Docket EPA-HQ-OW-2008-0068

Dear Water Docket:

AMWA appreciates the opportunity to comment on the preliminary regulatory determination for perchlorate as listed in the October 10, 2008 Federal Register (73 FR 60262). AMWA strongly

supports the process required by the 1996 Amendments of the Safe Drinking Water Act that places a strong emphasis on science and focuses on contaminants which: may have an adverse effect on humans, occur or are likely to occur at levels of public health concern and provide a meaningful opportunity for health risk reduction.

Members of Congress, the Administrator and the public have all weighed in on the need to regulate perchlorate. Concern over the lack of a regulatory path forward coupled with differing interpretations of the available scientific information has led to significant controversy. In such an environment, decisions need to be supported by peer reviewedscience to garner general acceptance. Accordingly, AMWA has several recommendations for the agency concerning peer review, review by the National Academy of Sciences (NAS), retention on the Contaminant Candidate List (CCL), the need for a strong cleanup standard, and other considerations. The remainder of these comments will address each in turn.

Peer-Review

In the Federal Register Notice, EPA expresses its intention to subject several key scientific points used in the decision process to peer-review before finalizing the determination. The agency notes that adjustments have been made to a previously peer-reviewed physiologically based pharmacokinetic (PBPK) model for predicting iodide uptake for several sensitive subpopulations. Additionally, the agency feels that it is pertinent to have a peer-review panel consider the appropriateness of the model for addressing non-adult populations. AMWA agrees that such reviews are appropriate and necessary. However, the agency should assure that peer review panel questions are posed so that the usefulness of the model is explored with specific regard to the most sensitive subpopulations. Specifically, detailed comment should be solicited on whether the lack of data on early fetal radioactive iodide uptake inhibition would be expected to affect the agency's determination that a Health Reference Level (HRL) of 15 ppb is protective of pregnant women and fetuses.

Response: See response to comment code 6400.

Commenter Name: Robert Howd
Commenter Organization: California Environmental Protection Agency, Water Toxicology Section
EPA Document ID: EPA-HQ-OW-2008-0692-1671
EPA Comment ID: 20645
EPA Comment Code: 6400

Comment: FROM: Robert A. Howd California Environmental Protection Agency, Office of Environmental Health Hazard Assessment

November 7, 2008

Water Docket Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Ave., NW Washington, DC 20460

Subject: Comments to Docket ID No. EPA-HQ-OW-2008-0068

To Whom It May Concern:

Thank you for providing the opportunity to comment on the Federal Register announcement of Friday, October 10, 2008, titled "Drinking Water: Preliminary Regulatory Determination on Perchlorate" (FR 73, no. 198, pp. 60262- 82). These comments were prepared by the Water Toxicology Section of the California Office of Environmental Health Hazard Assessment.

II(D), p 60265. EPA states that its regulatory determination on perchlorate has been based in part on a PBPK model with adjustments made by EPA that have not been peer reviewed (U.S. EPA, 2008). Some of the adjustments, including perchlorate inhibition of fetal iodide uptake, are critical to the interpretation. We recommend that such a peer review, plus opportunity for public comment on the model, be carried out before EPA publishes its final determination on perchlorate.

Response: See response to comment code 6400.

Commenter Name: Deborah Swackhamer
Commenter Organization: Science Advisory Board
EPA Document ID: EPA-HQ-OW-2008-0692-1749
EPA Comment ID: 20659
EPA Comment Code: 6400

Comment: November 5, 2008

The Honorable Stephen L. Johnson Administrator U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W. Washington, D.C. 20460

Dear Administrator Johnson:

Thank you for your memorandum of October 20, 2008, requesting that the Science Advisory Board (SAB) undertake a study to provide advice on how EPA can strengthen scientific assessments, better communicate the results of assessments, and integrate natural science assessment with economic and social assessments to support EPA decision making. I had the opportunity to discuss the request with my colleagues this week at a public advisory meeting of the chartered SAB. We will undertake this effort with the goal of providing advice to the new EPA Administrator within a year.

At our public meeting on October 28, 2008, the chartered SAB also discussed a draft report from the SAB's Drinking Water Committee on EPA's Draft Third Drinking Water Contaminant Candidate List (CCL3). The Committee's draft report highlighted its recommendation that perchlorate is one of four chemicals that "should be a high priority for consideration by the Agency, because there is a higher degree of certainty about their toxicity, occurrence, and treatability."

The SAB is also aware that EPA published a Drinking Water: Preliminary Regulatory Determination on Perchlorate in the Federal Register on October 10, 2008 (73 FR 60262-60282). That notice provides a preliminary determination that "a national primary drinking water regulation (NPDWR) for perchlorate would not present 'a meaningful opportunity for health risk reduction for persons served by public water systems'" and provides a thirty-day public comment period. The notice also states that EPA plans to issue a final regulatory determination by December 2008. It should be

noted that this preliminary determination relies on the use of a dosimetric model which is now undergoing letter peer review, and thus, its soundness will not be publicly vetted.

Given perchlorate's wide occurrence and well-documented toxicity to humans, the SAB strongly believes that there must be a compelling scientific basis to support a determination not to regulate perchlorate as a national drinking water contaminant. The quality of the scientific foundation for EPA's decisions depends on peer review, which brings a variety of scientific perspectives to bear on critical components of EPA's decisions. Where science assessments have been conducted with the benefit of external scrutiny, the end products have been better able to support the policy making process. This view is very much aligned with the perspectives expressed in your memorandum to the SAB.

Response: Administrator Stephen Johnson replied to the SAB on January 9, 2009. The letter is available in EPA's docket ID No. EPA-HQ-OW-2009-0297 for this notice. which is located in docket EPA-HQ-OW-2008-0692.

Commenter Name: Lynn Thorp
Commenter Organization: Clean Water Action
EPA Document ID: EPA-HQ-OW-2008-0692-2017
EPA Comment ID: 20851
EPA Comment Code: 6400

Comment: We are particularly concerned that the preliminary determination was issued before peer reviews of the physiologically-based pharmacokinetics (PBPK) model used to derive the health reference level AND the health reference level itself were available. Given widely varying analysis of existing data, these peer reviews could shed important light on the Agency's deliberations. We urge the Agency to reconsider its determination and to take the time necessary to fully consider setting a federal standard for perchlorate in drinking water.

I appreciate the opportunity to weigh in on this important decision and am happy to provide more information if required.

Sincerely, Lynn Thorp, National Campaigns Coordinator CC: Eric Burneson, OGWDW

Response: See response to comment code 6400.

Commenter Name: Caroline Baier-Anderson, PhD
Commenter Organization: Environmental Defense Fund
EPA Document ID: EPA-HQ-OW-2008-0692-1797
EPA Comment ID: 20949
EPA Comment Code: 6400

Comment: The Post hoc Application of PD Modeling Inappropriately Allows the Exceedence of the RfD

EPA has chosen to use a novel approach in setting a risk-based health risk level for perchlorate by using physiologically based pharmacokinetic modeling to justify the exceedence of the reference

dose at a level ranging from 2 - over 5%. In doing so, EPA would allow perchlorate exposures to attain unacceptably high levels.

The model that EPA is using has not yet completed peer review, so that stakeholders have no assurance that the model design is appropriate for the task at hand. EPA should wait until the peer review process is complete before applying this model for official purposes as the peer review process could uncover important limitations of the model. For instance, while the model reports that predicted perchlorate blood levels would be higher in the fetus, lactating women and neonates, it is not clear if the model includes new information regarding the impact of TSH on NIS uptake of perchlorate (e.g., Tran et al. 2008 is not cited in the EPA document describing the model, EPA/600/R-08/106A), nor is it known how this new information might affect the modeling results. A peer review panel would be in the best position to weigh in on questions such as this one.

It is also not clear if the model has been validated using responses of sensitive populations that include sub-optimal iodine intake. Given the documented impact on response to perchlorate exposure, this is would be an important step in the validation process. The model extrapolations were reportedly compared to data from the Chilean population, which as noted above, was fully iodine sufficient. Considering the demographics of iodine insufficiency in the US, it is imperative that the model extrapolations also be compared with data from a population that is not iodine sufficient.

Response: See response to comment code 6400.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20998
EPA Comment Code: 6400

Comment: Despite these conclusions, only one week later and without waiting for the report to be peer-reviewed and available for public comment, EPA announced that it would not regulate perchlorate in drinking water. Although the Federal Register notice does report the staff conclusions, it contradicts them concluding that "EPA believes drinking water with perchlorate concentrations at or below the HRL of 15 ug/L is protective of all subpopulations."[FN52: Id. at 60280]

Response: EPA has decided to regulate perchlorate in drinking water. See response to comment code 6120 and response to comment code 6400.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 21004
EPA Comment Code: 6400

Comment: First, such a determination is premature, since the Agency is still awaiting peer review comments on the HRL and has only just received peer review comments on the PBPK model.

Response: See response to comment code 6400.

EPA Comment Code: 6500 Comments on alternative risk reduction approaches

Individual Comments
Commenter Name: Richard T. Kloos
Commenter Organization: American Thyroid Association (ATA)
EPA Document ID: EPA-HQ-OW-2009-0297-0635
EPA Comment ID: 28530
EPA Comment Code: 6500

Comment: We are writing on behalf of the American Thyroid Association (ATA) in response to your request for comments (Fed Reg 74:41883, 08/19/09) regarding EPA's perchlorate regulatory determination. The ATA represents the largest and most established group of physicians dedicated to the study of the thyroid gland and its disorders.

Decreases in maternal thyroid hormone associated with even mild iodine deficiency may have adverse effects on the cognitive function of offspring.1,2,3 It has recently been suggested that mild iodine deficiency may also be associated with thyroid deficiency resulting in attention deficit and hyperactivity disorders in offspring.4 Iodine deficiency affects over 2.2 billion individuals worldwide (38% of the world's population), and iodine deficiency is the leading cause of thyroid failure causing preventable mental retardation worldwide.5

Over the last few decades, iodine intake in the United States has declined.6 Although iodine intake remains sufficient for the general U.S. population, there have been concerns in recent years that some pregnant women and women in their childbearing years may have inadequate iodine intake.7,8 For this reason, in 2006 the ATA published recommendations for iodine supplementation of all U.S. pregnant and lactating women.9 These guidelines have not been widely adopted, and the availability and frequency of use of iodine-containing prenatal multivitamin supplements among pregnant U.S. women remains suboptimal.10,11

Response: See response to comment ID 28842 under comment code 6500.
As discussed in detail in the final regulatory determination, EPA has found that perchlorate may have an adverse effect on human health.

Commenter Name: Richard T. Kloos
Commenter Organization: American Thyroid Association (ATA)
EPA Document ID: EPA-HQ-OW-2009-0297-0635
EPA Comment ID: 28532
EPA Comment Code: 6500

Comment: We would strongly urge that, whatever the EPA determines about the need for regulation of perchlorate in drinking water, attention should be paid to ensuring adequate iodine nutrition in the U.S., particularly among women who are pregnant or lactating.

Thank you for this opportunity to comment upon and contribute to your regulatory determination for perchlorate. Clearly, there is more need for studies in this area in order to obtain greater clarity.

Sincerely, Richard T. Kloos, M.D. Secretary/Chief Operating Officer, American Thyroid Association Co-Director, The Ohio State University Thyroid Cancer Unit Divisions of Endocrinology and Nuclear Medicine Columbus, OH. 43210-1296 Richard.Kloos@OSUMC.edu

Terry F. Davies, MB.BS, MD, FRCP, FACE President, American Thyroid Association Florence and Theodore Baumritter Professor of Medicine Mount Sinai School of Medicine One Gustave Levy Place, Box 1055 New York, NY 10029-6574

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Invited Editorial [see PDF docket ID EPA-HQ-OW-2009-0297-0635]

Response: See response to comment ID 28530 under comment code 6500.

Commenter Name: Stephen Haterius
Commenter Organization: National Association of State Departments of Agriculture (NASDA)
EPA Document ID: EPA-HQ-OW-2009-0297-0664

EPA Comment ID: 28549
EPA Comment Code: 6500

Comment: It is key to this discussion that exposure to perchlorate is only potentially problematic for individuals with iodine deficiency. There is no evidence[FN1: United States Food and Drug Administration. Perchlorate Questions and Answers. http://www.fda.gov/Food/FoodSafety/FoodContaminantsAdulteration/ChemicalContaminants/Perchlorate/ucm077572.htm] that iodine deficiency is a widespread problem in the United States, and that only individuals who are on restrictive diets or purposely avoid iodine consumption are at risk for such a deficiency. While there is no evidence that iodine deficiency is a widespread problem in the US, women of child-bearing age and pregnant women are theoretically more at risk for effects of perchlorate consumption. Because inadequate iodine consumption during pregnancy can lead to negative birth outcomes, any further reduction uptake by the thyroid from exposure to perchlorate could pose a risk. While there is no evidence of widespread iodine deficiency in women of child-bearing age or pregnant women, this subpopulation could be targeted with education about diet during pregnancy and appropriate prenatal care that stresses the importance of adequate iodine consumption during pregnancy.

In conclusion, we point to the EPA Office of Inspector General's (OIG) draft review[FN2: United States Environmental Protection Agency. Office Inspector General Scientific Analysis of Perchlorate. http://www.epa.gov/oig/reports/2009/20081230-2008-0010.pdf] of EPA's perchlorate assessment which emphasizes a number of important points that are relevant to this discussion. Specifically, the review points to the fact that other naturally occurring compounds found in food behave in a way that is similar to perchlorate. According to this review, regulating perchlorate in drinking water is unlikely to have any material impact on public health. We agree with the conclusion in OIG's draft that promoting adequate iodine intake is a superior approach than regulating perchlorate as a drinking water contaminant.

Because the public health concerns associated with potential perchlorate consumption can be addressed through education and dietary modifications in a small subset of the population, NASDA is very concerned that EPA not adopt an approach that would lead to consumer confusion, food scares, and potential financial devastation for American agricultural producers.

Sincerely, Stephen Haterius Executive Director

Response: See response to comment ID 28530 under comment code 6500. Perchlorate contamination is more widespread in foods than in drinking water; however, EPA does not believe that the widespread presence of perchlorate in food overrides the need for public health risk reduction for persons served by PWSs with perchlorate contamination. The Agency presented an extensive evaluation of dietary exposure to perchlorate in the October 2008 and August 2009 notices (73 FR 60262; USEPA 2008a and 74 FR 41883; USEPA 2009b). EPA has used this dietary exposure data to account for the relative source contribution (RSC) of perchlorate from food to estimate the range of levels of public health concern. EPA recognizes that a drinking water regulation would not eliminate total perchlorate exposure, but believes that the reduction in perchlorate exposure in drinking water presents a meaningful opportunity for health risk reduction for persons served by PWSs contaminated by perchlorate. EPA agrees that promoting iodide nutrition is good public health policy and may have a positive influence in reducing the iodide uptake inhibition effects associated with exposure to perchlorate. However, the Agency does not

think it is appropriate to rely on the promotion of iodide nutrition in this case, especially since these activities are outside of EPA's SDWA authority. As a result, while the health concerns associated with perchlorate may be addressed through other means, it is the Administrator's judgment that a standard limiting perchlorate in drinking water can reduce health risk, particularly to fetuses, infants and children.

Regarding the OIG report, while EPA acknowledges that nitrate and thiocyanate have the same mode of action as perchlorate, and that the effects of combined exposure to perchlorate, nitrate, and thiocyanate are additive, EPA does not believe there are sufficient scientific data currently available to assess and characterize the combined risk of these contaminants. EPA has committed to a drinking water strategy that outlines four principles to expand public health protection for drinking water (USEPA, 2010b). One of these principles is to address contaminants as groups. However, EPA does not believe that regulatory action to address perchlorate should be further delayed. Therefore, EPA intends to develop a proposed rule for perchlorate. At such time as a NPDWR is promulgated, EPA is required to review and revise, as appropriate, its drinking water standards at least every six years. Any revision must at least maintain or improve public health protection. When there are sufficient scientific data to assess the cumulative risks of perchlorate and other contaminants, EPA will review this information to evaluate whether any revisions of NPDWRs are appropriate.
EPA has determined the need to regulate perchlorate in drinking water. Care will be taken to communicate the implications of that regulation.

Commenter Name: John P Gibbs
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0636
EPA Comment ID: 28555
EPA Comment Code: 6500

Comment: Efforts to assure adequate iodine in prenatal vitamins and infant formulas as suggested by the draft OIG report offer the most reasonable and immediate protection from the presence of NIS inhibitors among the recognized sensitive subpopulations.

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Response: See response to comment ID 28530 under comment code 6500.

Commenter Name: Sonia Salas
Commenter Organization: Western Growers Association on behalf of several California agriculture groups
EPA Document ID: EPA-HQ-OW-2009-0297-0652
EPA Comment ID: 28681
EPA Comment Code: 6500

Comment: For iodine, FDA found that each of the 14 age/sex groups, including infants, children, and women of childbearing age exceeded the average intake levels estimated by the NAS to meet requirements for healthy individuals.

In light of these findings, FDA continues to stand by its prior recommendation that consumers should not alter their infants' and children's diets or eating habits. Indeed, many of the foods at issue are major dietary sources of iodine and other nutritionally essential substances.

EPA's Calculation of the Relative Source Contribution for its 2008 Preliminary Regulatory Determination also Reveals that Perchlorate Exposure from Food is Below any Meaningful Level of Concern.

Response: EPA calculated potential alternative HRLs that were included in the August 2009 notice. These values incorporate and estimate perchlorate from food, deriving the potential alternative HRL such that only the water contribution of perchlorate would require adjustment to attain a tolerable perchlorate exposure from all sources. The Agency presented an extensive evaluation of dietary exposure to perchlorate in the October 2008 and August 2009 notices (73 FR 60262; USEPA 2008a and 74 FR 41883; USEPA 2009b). EPA has used this dietary exposure data to account for the relative source contribution (RSC) of perchlorate from food to estimate the range of levels of public health concern. EPA recognizes that a drinking water regulation would not eliminate total perchlorate exposure, but believes that the reduction in perchlorate exposure in drinking water presents a meaningful opportunity for health risk reduction for persons served by PWSs contaminated by perchlorate.

Commenter Name: Tom Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0415
EPA Comment ID: 28842
EPA Comment Code: 6500

Comment: AWWA also concurs with the Agency's Inspector General [FN1: Wilson, M. 2008. Scientific Analysis of Perchlorate. US Environmental Protection Agency, Office of Inspector General. Available at http://www.epa.gov/oigearth/reports/2009/20081230-2008-0010.pdf] in stating that regulatory action under the Safe Drinking Water Act (SDWA) is not the appropriate or effective way to address the overarching public health issue - iodide deficiency. The National Research Council (NRC) assessment [FN2: National Research Council (NRC). 2005. Health Implications of Perchlorate Ingestion. National Academy Press, Washington, DC.] of perchlorate also recognized iodide deficiency as the larger public health issue.

Response: EPA based its final regulatory determination on a number of different factors including the careful consideration of public comments. Regarding correcting iodine deficiencies, the Food and Drug Administration and Centers for Disease Control generally conclude that there is sufficient iodine in the diet. Below are findings from FDA's Total Diet Study (2003-2004) that estimates the dietary intake of iodide for 14 age-sex groups (Murray et al., 2008) and CDC's National Health and Nutrition Examination Survey that measured perchlorate in the urine of study participants in (2003-2004, no data on < age 6). FDA's Total Diet Study findings: - Infants, 6-11 months, exceeded their Adequate Intake - Children and adult age/sex groups exceed their relevant Estimated Average Requirement CDC's National Health and Nutrition Examination Survey: - "This finding confirms the stability of the U.S. iodine intake and continued adequate iodine nutrition for the country in general." - "On the basis of median urinary iodine concentrations, iodine intake of women of childbearing age appears adequate."

EPA Comment Code: 7000 Miscellaneous Comments

Response to Code 7000: See response to comment code 6120 for a discussion of EPA's decision to regulate perchlorate in drinking water and initiate the development of a proposed national primary drinking water regulation. EPA received a number of comments in response to its preliminary regulatory determination for perchlorate(73 FR 60262, October 10, 2008) and the supplemental request for comment on the perchlorate regulatory determination (74 FR 41883, August 19, 2009) that were not directly related to the Agency's decision to regulate perchlorate in drinking water. These comments are compiled in response to comment code 7000 in this response to comment document. EPA is not directly addressing comments that do not relate to the Agency's decision on whether or not the Agency should promulgate a national primary drinking water regulation (NPDWR) for perchlorate under the Safe Drinking Water Act (SDWA). SDWA provides EPA with the authority to regulate public water systems through national primary drinking water regulations. Under this authority EPA plans to propose and promulgate a regulation that public water systems will have to comply with through monitoring and potentially using treatment techniques to reduce the levels of perchlorate in the drinking water they supply to their customers. The authority under SDWA does not apply to discharges, improper disposal or other releases of perchlorate or other contaminants. EPA therefore is not addressing comments related to these concerns under this action. EPA is also not addressing comments related to contaminants other than perchlorate or drinking water policies unrelated to the perchlorate regulatory determination.

Individual Comments
Commenter Name: W Zielke
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0332
EPA Comment ID: 19818
EPA Comment Code: 7000

Comment: We should be finding out how Perchlorates are getting into our water and take steps to prevent that from happening.

Response: See response to comment code 7000.

Commenter Name: Margaret Baco
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0624
EPA Comment ID: 19978
EPA Comment Code: 7000

Comment: Further, there is an urgent requirement to safeguard public health through effective legal action requiring the provision of reliable tap water filters in all public establishments, inclusive of tax relief measures. All public schools, hospitals and restaurants should be equipped with this safeguard immediately to reduce the risk of further exposure.

Further, new programs must be established to ensure that private homes are able to afford installation of effective water filters.

Further, legal actions must be established to regulate and control the collection of appropriate disposal of such filters.

Sincerely,

Margaret Baco

Response: See response to comment code 7000. NSF International, the Water Quality Association and other independent certification organizations have certified household treatment systems for perchlorate removal.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0839
EPA Comment ID: 20108
EPA Comment Code: 7000

Comment: PEACELOVE EARTHHEART

Response: This is not a comment, a response is not necessary.

Commenter Name: L. L. Schumacher
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-0664
EPA Comment ID: 20239
EPA Comment Code: 7000

Comment: And what about the highly toxic fumigant you approved for use on strawberries exactly 1 year ago, for one year. Are you going to make that permanent? I would venture to say yes because the "money grubbers" want it and you always rule in their favor.

You should change your name from the Environmental Protection Agency, to the Environmental Destruction Agency.

Yours truly, Leonard L. Schumacher

Response: See response to comment code 7000.

Commenter Name: Ed Thomas
Commenter Organization: National Rural Water Association
EPA Document ID: EPA-HQ-OW-2008-0692-1669
EPA Comment ID: 20621
EPA Comment Code: 7000

Comment: In closing we find it inexplicable that the Agency was able to interpret the statutory standard of what determines the "meaningful opportunity for health risk reduction" and make a determination in a relative short period of time. But, on the other hand, the Agency has not been able to interpret nor make a determination on similar statuary standards of "unreasonable risk to

health" (URTH) [42USC300g-5(a)(3)] or "protective of public" [42USC300g-1(b)(15)(B)]. What we find inexplicable is that the determination EPA has failed to make heretofore is more pressing to community water supplies than the determination EPA recently made for perchlorate. We believe that EPA should identify the URTH levels and what constitutes "protective of public health".

We thank you for the opportunity to provide comments regarding this important matter.

Sincerely,

Ed Thomas

Electronic Attachments: 1. Rubin trade off health risk final.pdf

Response: See response to comment code 7000.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-1748
EPA Comment ID: 20658
EPA Comment Code: 7000

Comment: Finally, if the SAB convenes any public meeting on perchlorate, the PSG would welcome an opportunity to present the scientific literature and our public comments. For over 10 years, the PSG has worked cooperatively with EPA, states, and other Federal agencies to provide the best available scientific information on perchlorate to assist public agencies. We look forward to any such opportunity with the SAB.

Sincerely,

Mr. Michael Girard Chairman Perchlorate Study Group

Cc: Marcus Peacock, Deputy Administrator Benjamin Grumbles, Assistant Administrator, Office of Water Cynthia Dougherty, Director Office of Ground Water and Drinking Water Eric Burneson, Chief, Targeting and Analysis Branch Suhair Shallal, SAB Designated Federal Officer

Response: There will be future opportunities to provide input/submit comments during development of a proposed NPDWR for perchlorate.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1743
EPA Comment ID: 20685
EPA Comment Code: 7000

Comment: The perchlorate contamination in Tewksbury, MA a few years ago resulted in 75% of my household not being able to consume our municipally provided tap water. My two children (both under age 2) and my pregnant wife were in the 'high risk' group that were advised not to consume or brush their teeth with the contaminated water. Standard commercially available water

filtration systems were either a) incapable of addressing the contaminant or b) unable to remove perchlorate contaminants to any particular standardized safe level. The filtration systems reviewed included systems that used reverse osmosis filtration as their buy-in into the organization.

Response: See response to comment code 6120. NSF International, the Water Quality Association and other independent certification organizations have certified household treatment systems for perchlorate removal.

Commenter Name: Y. Carbajal
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1847
EPA Comment ID: 20736
EPA Comment Code: 7000

Comment: It is in everyone's best interest that drink water be tested for containments. Failure to do so can lead to a catastrophic epidemic.

Response: See comment code 7000.

Commenter Name: R. Howard
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1848
EPA Comment ID: 20737
EPA Comment Code: 7000

Comment: UR KILLING US THANK FOR THE WONDERFUL 8YRS MR.PRES IHOPE UR LIFE ISNT AS LONG AS THESE 8YRS HAVE BEEN

Response: This is not a comment, a response is not necessary.

Commenter Name: J Bennet
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-1860
EPA Comment ID: 20744
EPA Comment Code: 7000

Comment: 11/06/08

Dear EPA,

Please get toxins out of our water.

J. Bennet 211 Royal St. Alexandria, VA 22314

Response: See response to comment code 7000.

Commenter Name:
Commenter Organization: The Night Move, LLC

EPA Document ID: EPA-HQ-OW-2008-0692-1960
EPA Comment ID: 20808
EPA Comment Code: 7000

Comment: As a new business in Michigan, we have taken the initiative to show concern for the environment in every way we can. We collectively look for ways to reduce our negative impact on the environment and search for ways to improve it. The Night Move started on the premise to get people out of their cars and into public transportation, reducing the air pollution from car exhaust. Also, we run our bus on biodiesel to reduce our emissions. For the emissions we do put out, we have partnered with CarbonFund.org to neutralize our carbon footprint. We don't stop there. Our flyers and advertisements are printed on recycled paper, passenger trash is recycled, and we reuse water to clean the bus. Of course, there are always ways to improve and we are always looking for them. We do this because we know what we do has an impact on the environment around us. This means we are impacting the people around us whether they use our services or not. We like to do our part to keep our environment clean and safe to live in, and we expect others to be just as courteous, especially our government.

Response: This is not a comment, a response is not necessary.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2007
EPA Comment ID: 20837
EPA Comment Code: 7000

Comment: DIRTY LAKES!! Don't do this!!!

CLEAN LAKES!!

Keep our Lakes Clean!!!

[See illustration in PDF EPA-HQ-OW-2008-0692-2007]

Response: See response to comment code 7000.

Commenter Name: Brien Beebe
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2011
EPA Comment ID: 20843
EPA Comment Code: 7000

Comment: 11/6/08

I WOULD LIKE TO BELIEVE THAT THE EPA WOULD FIGHT TO PROTECT FOR CLEAN WATER AND "PROTECT OUR ENVIRONMENT."

BRIEN BEEBE 311 DUKE ST. ALEXANDRIA VA. 22314

Response: See response to comment code 7000.

Commenter Name: B.K.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2012
EPA Comment ID: 20844
EPA Comment Code: 7000

Comment: 11/06/08

Dear EPA,

Toxins out of water.

BK 207 S. Royal Alexandria, VA 22134

Response: See response to comment code 7000.

Commenter Name: Lynn Thorp
Commenter Organization: Clean Water Action
EPA Document ID: EPA-HQ-OW-2008-0692-2017
EPA Comment ID: 20849
EPA Comment Code: 7000

Comment: December 1, 2008

Stephen L. Johnson Administrator U.S. Environmental Protection Agency Washington DC 20460

Dear Administrator Johnson,

I am writing on behalf of Clean Water Action and it's 1.2 million members. Due to clerical errors, our organization's signature was not affixed to comments on the Agency's preliminary determination on perchlorate which were prepared and submitted by the Natural Resources Defense Council for the relevant docket. I want to draw your attention to our organization's support for these comments despite our signature not being on the official docket copy.

Response: The commenter's support for comments prepared by the Natural Resources Defense Council (comment letter ID EPA-HQ-OW-2008-0692-1988) is noted.

Commenter Name: Lenny Siegel
Commenter Organization: Center for Public Environmental Oversight
EPA Document ID: EPA-HQ-OW-2008-0692-2019
EPA Comment ID: 20855
EPA Comment Code: 7000

Comment: This reminds me of O.J. Simpson's criminal defense. He insisted that some third party or parties killed his wife and Ronald Goldman, but he showed little interest in finding the unknown perpetrators.

Response: No response necessary to the information provided by the commenter.

Commenter Name: Ron Curry
Commenter Organization: New Mexico Environment Department
EPA Document ID: EPA-HQ-OW-2008-0692-1796
EPA Comment ID: 20934
EPA Comment Code: 7000

Comment: In considering these comments, particularly this groundwater monitoring data, it is important for EPA to understand that New Mexico is very dependent on its groundwater resources for drinking water. New Mexico is an arid state, with relatively little surface water. New Mexicans obtain approximately 90 percent of their drinking water from groundwater aquifers.[FN11: Affidavit of William Olsen, Chief, Ground Water Quality Bureau, N.M. Environment Dep't, at 3, In re Appeal of Supplemental Discharge Permit for Closure (DP-1341) for Phelps Dodge Tyrone, Inc. (N.M. Water Quality Control Comm'n July 9, 2007) (Nos. WQCC 03-12(A) and WQCC 03-13(A)).] And New Mexico is growing and developing rapidly, placing greater demands on its aquifers. According to the New Mexico State Demographer at the University of New Mexico Bureau of Business and Economic Research, the population of New Mexico is expected to increase by 30 percent between 2005 and 2020, and by more than 50 percent between 2005 and 2035.[FN12: University of New Mexico, Bureau of Business and Economic Research, Population Projections for New Mexico and Counties, available at www.unm.edu/~bber. The information was confirmed in a telephone conversation with Adelamar N. Alcantera, Ph.D., New Mexico State Demographer, on November 24, 2008.] We therefore assume that much of the State's groundwater will be used for drinking water in the future. Consequently, there is a substantial likelihood that this perchlorate contamination will occur in public water systems in the foreseeable future.

Response: See response to comment code 7000.

Commenter Name: Herwig Opdebeeck
Commenter Organization: Opdebeeck Consulting
EPA Document ID: EPA-HQ-OW-2008-0692-1798
EPA Comment ID: 20955
EPA Comment Code: 7000

Comment: RE: Docket ID No. EPA-HQ-OW-2008-0068

Comments on the US Environmental Protection Agencyâ€™s Preliminary Regulatory Determination on Perchlorate November 28th, 2008

Comment on the USEPA Office of Waterâ€™s Preliminary Regulatory Determination on Perchlorate.

Comment subjects

1. Relative Source Contribution (RSC) EPAâ€™s past RSC based on a "default" assumption versus EPAâ€™s RSC used in this Preliminary Regulatory Determination

2. The very particular case of perchlorate: Total effective equivalent perchlorate NOEL and RfD

3. Checking of some outcomes of this EPA preliminary determination with those obtained trough another road.

Response: This is not a comment, a response is not necessary.

Commenter Name: Jennifer Sass, PhD.
Commenter Organization: Natural Resources Defense Council
EPA Document ID: EPA-HQ-OW-2008-0692-1988
EPA Comment ID: 20996
EPA Comment Code: 7000

Comment: E. A final MCL below 1 ppb is both technologically and economically feasible.

Technical Feasibility

U.S. EPA's Method 314 approved ion chromatography detection protocol, for example, routinely detects perchlorate pollution at levels of 0.2ppb and the State of Massachusetts has established a 'reportable concentrations level for perchlorate of 2 ppb.[FN46: Thorne, Philip G. Field Screening Method for Perchlorate in Water and Soil, ERDC/CRREL Technical Report 04-8, 36 pp, Apr 2004.],[FN47: "Final Changes to the Massachusetts Contingency Plan -310 CMR 40.0000," downloaded from http://www.mass.gov/dep/cleanup/laws/perchlorate-310CMR40-07282006.pdf, November 2 2006.] Ion exchange technology is able to treat perchlorate contamination to levels considerably below 1 ppb. Treatment systems operating on perchlorate- impacted wells owned by Aquarion Water Company in Massachusetts, for example, treat wells to below 1 ppb.[FN48: "US Filter Recovery Services," downloaded from www.usfilter.com, November 2 2006.]

Economic Feasibility

The cost of complying with a perchlorate Maximum Contaminant Level of less than 1 ppb for the City of Rialto - one of the most impacted water systems in California - for example will be zero after cleanup costs are recovered from identified responsible parties. A complete economic feasibility study should also include an analysis of the costs associated with healthcare and lost work resulting from illnesses associated with perchlorate contaminated water.

Response: See response to comment code 6120. Feasibility and health risk reduction and cost analyses will be performed in support of a proposed National Primary Drinking Water standard.

Commenter Name: Michael Girard
Commenter Organization: Perchlorate Study Group
EPA Document ID: EPA-HQ-OW-2008-0692-2082
EPA Comment ID: 21025
EPA Comment Code: 7000

Comment: Your letter also highlights states which have issued MCLs, including California, Massachusetts, and New Jersey (which has proposed, but not finalized a standard.)

As your letter points out, several states have issued standards or taken other regulatory steps relating to perchlorate in drinking water.. That is a separate issue from whether a national standard is advisable.

The Association of State Drinking Water Administrators noted in their recently filed comments that "States are generally in favor of EPA's decision not to regulate, but there are some states that do favor a national regulation on perchlorate, especially those who have already set their own standard."[FN7: Association of State Drinking Water Administrators, Letter to EPA Docket, Docket EPA-HQ-OW-2008-0692, Nov. 10, 2008.] The American Water Works Association, the largest organization of water supply professionals in the world, announced its agreement with EPA's preliminary determination, based upon the results of two independently commissioned assessments which support EPA decision. [FN8: American Water Works Association, Drinking Water: Preliminary Regulatory Determination on Perchlorate Docket EPA-HQ-OW-2008-0692; Nov. 10, 2008.]

Response: See response to comment code 7000.

Commenter Name: Teresa Jordan
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2086
EPA Comment ID: 21108
EPA Comment Code: 7000

Comment: Mr. Grumbles and Mr. Burneson, it is imperative that the USEPA, in Federal Register notices and in the Agency's Website, provide a facsimile number for the interested persons to submit written comments. I do not E-mail. I do not always have transportation to get to the post office. Foot problems keep me from walking long distances. Since I have a fax machine, I am able to submit comments not only to members of Congress, but State and Federal government elected officials, and agenices. All public comment submittal tools must be made available. The USEPA by doing otherwise limits the public's right to comment on issues.

Mr. Grumbles and Mr. Burneson, I notice that the USEPA provides an avenue to help the hearing impaired population participate. How does the USEPA help the visually impaired population participate in the public comment process?

Response: EPA acknowledges the commenter's request. In the future, written comments may be submitted to EPA's Docket Center Public Reading Room at the following fax number: 202-566-9744. Please include the appropriate Docket ID No. with your submission.

Commenter Name: Philip Hoos
Commenter Organization: Earthjustice
EPA Document ID: EPA-HQ-OW-2008-0692-2111
EPA Comment ID: 21137
EPA Comment Code: 7000

Comment: To whom it may concern,

I would like the attached document to be posted in docket number EPA-HQ- OW-2008-0692. Please disregard my previous email where I provide the incorrect docket number. If you have any questions please feel free to email me.

Thank you for your time, Phil

Phillip Hoos Research Associate Earthjustice 426 17TH St., 5th Floor Oakland, CA 94612 T: 510-550-6700 F: 510-550-6740 www.earthjustice.org

Because the earth needs a good lawyer

[please see attachment PDF Docket ID EPA-HQ-OW-2008-0692-2111]

Response: The attachment has been posted to docket number EPA-HQ- OW-2008-0692.

Commenter Name: Charlotte L. Sherry
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2119
EPA Comment ID: 21989
EPA Comment Code: 7000

Comment: Water Docket, EPA Mailcode 2822T 1200 Pennsylvania Ave., Washington, D.C. 20460

We have lived in Gambrills area since 1969. Lately when I make coffee, hot tea, ice tea or something similar it has an odor and taste of chorine in it.

The water line has broken twice in the same place in the last few years. All these pipes have to be old and need to be checked for cracks that let contamination into our water.

Thank you, Charlotte L. Sherry

Response: See response to comment code 7000.

Commenter Name: David L. Louden
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2161
EPA Comment ID: 22091
EPA Comment Code: 7000

Comment: 21 November 2008

STATEMENT FOR THE RECORD

Subj: CLEAN WATER ACTION I CO DOCKET ID NO. EPA-HQ-OW-2008-0692

Dear Sir/Madame;

I wish it to be known that I support the testing, both routine and sustained, of water delivered by public, state or county for purposes of drinking, cooking, cleaning, bathing or their kind.

The Environmental Protection Agency operates as a public trust on behalf of the citizens of the United States. It is therefore both a custodial responsibility as well as a matter of good stewardship to perform all due diligence in the execution of the duties and responsibilities assigned to the EPA by the laws and directives of the United States. I wish you continued success as you carry out this mandate on behalf of your fellow citizens.

Kind regards, David L. Louden 7894 Bastille Pl Severn, MD 21144 410 551 7866 davidlouden@hotmail.com

Response: See response to comment code 6120.

Commenter Name: John A. Forbes
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2162
EPA Comment ID: 22092
EPA Comment Code: 7000

Comment: November 18, 2008

Dear EPA Administrator Stephen Johnson

I write to your with an urgent request to regulate greenhouse gas emissions under the Clean Air Act.

Greenhouse gases are a serious threat to public health and people's welfare especially small children. The US must again take the lead on the issue at the Federal level.

The Supreme Court affirmed to EPA authority. I urge you to regulate by setting specific emission reduction standards for power plants, big factories, vehicles and fuels.

Please act John A Forbes III

Response: See response to comment code 7000.

Commenter Name: Thomas S Soell
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2184
EPA Comment ID: 22378
EPA Comment Code: 7000

Comment: 13 Nov 2008

To whom it may concern,

I fortunately live next to the Herald Harbor water tower in Crownsville, Maryland. Every year we get a report on the level of contaminants found in the drinking water supplied by this source. It would

be interesting to at least know the level of perchlorates in the water. I have no idea how to test for perchlorates or what level is safe or not. If they are harmful, it would be nice to know what levels they are in our water.

Thanks for your attention to this matter!

Thomas S. Soell 485 Mountain Rd Crownsville, MD 21032

Response: See response to comment code 6120. You may want to call your drinking water utility or state drinking water program to learn the results of past monitoring or to find out if monitoring is required in your state. If there is no requirement for monitoring in your state, you can have your water analyzed by a laboratory that is certified for the analysis of perchlorate or similar compounds. An EPA website provides a list of state certification officers or links to certified laboratories in your state.

Commenter Name: Sean Auth
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2212
EPA Comment ID: 22414
EPA Comment Code: 7000

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

As an idealistic youth, I like to believe that those who are in charge hold the interests of those it is their duty to protect above those of big business, in the face of the apathetic and corrupt. We already have to worry about enough epidemics affecting the women and children of this nation, please do your part to shorten the list, if not for my family then for yours.

Sincerely, Sean Auth 619 Bates College Lewiston, ME 04240

Response: See response to comment code 6120.

Commenter Name: Hal Hyman
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2280
EPA Comment ID: 22487
EPA Comment Code: 7000

Comment: Docket # EPA-HQ-OW-2008-0692 Environmental Protection Agency Mailcode: 2822T, 1200 Pennsylvania Ave., NW Washington, 20460

Dear Administrator Johnson and EPA staff,

The NRDC is a radical group who are for the destruction of the United States disguised as environmentalism. It is Marxism.

BE AWARE AND DESTROY THEIR AGENDA

Sincerely, Hal Hyman 49 Price Avenue Erlanger, KY 41018

Response: This comment is not relevant to this action.

Commenter Name: Under 13
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2085
EPA Comment ID: 24975
EPA Comment Code: 7000

Comment: Dear Water people,

I like clean water because we drink it. I would not like to drink dirty water. People in Africa have dirty water and are dying and they are not very happy.

Love, [comment from patron under the age of 13]

Response: See response to comment code 7000.

Commenter Name: Kraig Erickson
Commenter Organization: RMC Water and Environment (RMC)
EPA Document ID: EPA-HQ-OW-2008-0692-2299
EPA Comment ID: 24980
EPA Comment Code: 7000

Comment: Currently my company, RMC, is working with Pasadena Department of Water and Power to address high percholate levels in the Monk Hill area. Windsor Reservoir is a potable water storage reservoir constructed in the early 1900s with a capacity of 4.75 million gallons. It went out of service due to high percholate levels in the groundwater from wells feeding the Reservoir. PWP is currently constructing a percholate treatment facility at Reservoir site. Please feel free to contact me if you would like more information regarding PWP's actions to address percholate plumes.

Kind regards, - Kraig Erickson Project Engineer RMC Water and Environment 2400 Broadway, Suite 300 Santa Monica, CA 90404 Phone: 310-566-6460 Fax: 310-566-6461 KErickson@rmcwater.com http://ww.rmcwater.com Innovative Solutions for Water and the Environment

Sincerely, Kraig Erickson 2400 Broadway Suite 300 Santa Monica, CA 90404

Response: See response to comment code 7000.

Commenter Name: Under 13
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2008-0692-2337
EPA Comment ID: 25017

EPA Comment Code: 7000

Comment: Dear E.P.A,

I want clean drinking water!

From, [comment from patron under the age of 13]

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0073
EPA Comment ID: 28350
EPA Comment Code: 7000

Comment: ARE YOU KIDDING????????THIS IS A NO BRAINER! DON'T WE HAVE ENOUGH AUTO IMMUNE DISEASES AND CANCER CAUSING SUBSTANCES IN OUR LIVES? ISN'T THE WORD 'PROTECTION' IN THE ENVIRONMENTAL PROTECTION AGENCY THE CLUE THAT YOUR AGENCY IS SUPPOSED TO PROTECT US FROM ANY CONTAMINANTS??? PLEASE WAKE UP NOW!!!!!

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0090
EPA Comment ID: 28353
EPA Comment Code: 7000

Comment: PLEASE CONSIDER YOUR CHILDREN,GRANDCHILDREN, AND GREAT-GRAND CHILDREN WHEN TALKING ABOUT THIS CONTAMINATION OF OUR/THEIR DRINKING WATER. IT SHOULD BE SO ELEMENTARY OF A DECISION NOT TO ALLOW THE CONTAMINATION OF DRINKING WATER REGARDLESS OF MONETARY OR POLITICAL INFLUENCES. DO WHAT IS MORALLY JUST. PROTECT THE NATURAL RESOURCE WE WERE ENTRUSTED WITH;DON'T CONTAMINATE IT AND HOPE IT WILL BE SATISFACTORY.

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0118
EPA Comment ID: 28358
EPA Comment Code: 7000

Comment: This has got to be a joke right? Plain and simple...would the EPA be drinking

Response: See response to comment code 7000.

Commenter Name: J. Clarke
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0125
EPA Comment ID: 28361
EPA Comment Code: 7000

Comment: this really seems like a no brainer. we need to start acting on simple things like this in order to protect our future. with the onset of droughts throughout the US, we need to begin protecting what we do have before it's too late.

thanks,j. clarke

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0134
EPA Comment ID: 28363
EPA Comment Code: 7000

Comment: Please keep our waters safe!

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0157
EPA Comment ID: 28373
EPA Comment Code: 7000

Comment: This is really angering me, I may not be 18 yet and a legal adult, but i have as much right as any to drink UNCONTAMINATED water! this isnt the only problem too with drinking water! It has recently been recognized as of sept. 12th (today actually) in the new york times how all across the nation people can't even drink their tap water because there are contaminants from coal companies in them. The water has been found to contain barium, arsenic, lead, magenese, and other harmful chemicals. People get ugly and painful rashes just by letting it touch their skin and have to apply a special lotion after showing because it makes their skin BURN. A 6 year old boy was brought to the dentist and had to get metal caps on his teeth because the water had eaten away the enamel from his molars!

Government needs to address this because it is a fundamental living need- water. if we could ensure safely in our tap water, we could stop spending 10 billion dollars a year BOTTLING the stuff and just have people use a reusable safe stainless steel or hard safe-plastic bottle and save our ocean lots of pollution. Hey government! have uy heard there is a GIANT dump in the middle of the pacific ocean, circulating at a growing size that is already twice the size of Texas?!

Start addressing the things that really matter

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0165
EPA Comment ID: 28376
EPA Comment Code: 7000

Comment: AIRPLANES DUMP FUEL EACH TIME THEY LAND & USUALLY OVER WATER ,INCLUDING DRINKING WATER . WE NEED TO PURIFY OUR DRINKING WATER BETTER TO REMOVE CONTAMIN ATES LIKE "PERCHLORATE" .

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0179
EPA Comment ID: 28384
EPA Comment Code: 7000

Comment: Our water is more important than most of us know. Keeping polutants such as jet fuel out of the water is crucial. We have so many more cancers, birth defects, and illnesses than ever before, it's not a difficult stretch to believe our water quality is part of the problem. Please tighten water quality regulations today.

Response: See response to comment code 7000.

Commenter Name: Charyl Curry Gargel
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0216
EPA Comment ID: 28390
EPA Comment Code: 7000

Comment: I am a very concerned business owner and citizen that is very concerned about our drinking water.Documents are showing an extremely dangerous amounts of the agent PERCHLORATE going into our aquafiers.Please investigate and take remediation action to correct this for the sake of our citizens.

Thank You Charyl Curry Gargel

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0240
EPA Comment ID: 28418

EPA Comment Code: 7000

Comment: Hey, let's PROTECT the water supply and not bow to corporate interests that want to make money at the expense of public health.

Response: See response to comment code 7000.

Commenter Name: Terrence O'Brien
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0302
EPA Comment ID: 28433
EPA Comment Code: 7000

Comment: I have been involved in Pharmaceutical manufacturing for over 25 years. I, more than most people, appreciate the potential impact that even minute quantities of chemical compounds can have on peoples health. Please pursue polluters and protect innocent consumers of this country. That is why your organization was created. I shouldn't have to worry about Perchlorate, MTBE or other industrial compounds in my drinking water.

Sincerely, Terrence O'Brien Louisville, CO

Response: See response to comment code 7000.

Commenter Name: Sandra Chamberlin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0306
EPA Comment ID: 28434
EPA Comment Code: 7000

Comment: What is more basic and necessary than to have safe, clean drinking water. We must do everything for ourselves and our children, to protect rather than pollute our water. No one should have the right to harm others! Drinking is not a choice, it is life itself. Please help reverse the damage we've done and do not continue to contaminate.

Thank you , Sandra Chamberlin Montclair, NJ 07042 21 Edgewood Rd.

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0308
EPA Comment ID: 28436
EPA Comment Code: 7000

Comment: Keep our waters clean, for our children and families!

Response: See response to comment code 7000.

Commenter Name: D. Reynaud
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0319
EPA Comment ID: 28441
EPA Comment Code: 7000

Comment: Please give us more strongly enforced protections for our nation's water supplies!

Response: See response to comment code 7000.

Commenter Name: John Bachalis
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0344
EPA Comment ID: 28449
EPA Comment Code: 7000

Comment: I don't understand why there should be any question of whether we should keep any kind of poisons out of our drinking water. Don't we all need water to live? I see no reason for harmful chemicals or any kind, governmental or commercial to be allowed in our waters.

Do your job, and keep our water, air and land free of poisons.

John Bachalis, Yardley, PA 19067-1617

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0351
EPA Comment ID: 28452
EPA Comment Code: 7000

Comment: It defys logic that this discussion is happening. Because it is poison it is driving medical costs. With 17% of GDP going to medical, and that has gone up 1% since I have been following the number over the last five years, where have you been? You need to be looking at Periodic Table metals to really solve societal issues, What are my taxes paying for, a debate on how poison is poison? Commen sense people, not hogwash is needed from people that I pay.

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0358
EPA Comment ID: 28454
EPA Comment Code: 7000

Comment: It is absolutely ludicrous to allow toxic poison in our drinking water.

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0362
EPA Comment ID: 28456
EPA Comment Code: 7000

Comment: How does a harmful chemical that comes from rocket fuel get in so many public waterways? Where is this rocket fuel made? Why are we eventually bathing and drinking it?

Response: See response to comment code 7000.

Commenter Name: Larry Ladd
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0372
EPA Comment ID: 28458
EPA Comment Code: 7000

Comment: I have already submitted comment 80a1871f, and I would like that comment to be attributed to myself, Larry Ladd, rather than "anonymous." I also would like to make a correction to the above
Comment: "with the parvovirus outbreaks in Dharan after Patriot missile deployment, Badr 2002 pmed 11938419," should read "with the parvovirus outbreaks in Dharan after Patriot missile deployment, Mallouh & Qudah 1995 pmed 7715986."

Larry Ladd 11064 Santiam River Court Rancho Cordova CA 95670 http://www.perchlorate.org

Response: EPA has made these corrections.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0374
EPA Comment ID: 28459
EPA Comment Code: 7000

Comment: Please, we let so much garbage into our food supply; excrement in meat, pesticides, growth hormones, at least keep the water as pure as possible! Spare no expense to ensure it stays that way

Response: See response to comment code 7000.

Commenter Name: Ruth Neifeld
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0402
EPA Comment ID: 28468
EPA Comment Code: 7000

Comment: I do not know if this note is addressed to the correct agency. I am writing to ask that you help all Americans by ensuring that our drinking water is safe. I have been reading of many instances where this is not the case. We need someone in government to take on this task.

Thank you for your interest. Ruth Neifeld

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0406
EPA Comment ID: 28469
EPA Comment Code: 7000

Comment: I support limiting chemicals in our drinking water.

Response: See response to comment code 7000.

Commenter Name: Ed Thomas
Commenter Organization: National Rural Water Association (NRWA)
EPA Document ID: EPA-HQ-OW-2009-0297-0521
EPA Comment ID: 28477
EPA Comment Code: 7000

Comment: In closing we find it inexplicable that the Agency was able to interpret the statutory standard of what determines the "meaningful opportunity for health risk reduction" and make a determination in a relative short period of time. But, on the other hand, the Agency has not been able to interpret nor make a determination on similar statuary standards of "unreasonable risk to health" (URTH) [42USC300g-5(a)(3)] or "protective of public" [42USC300g-1(b)(15)(B)]. What we find inexplicable is that the determination EPA has failed to make heretofore is more pressing to community water supplies than the determination EPA recently made for perchlorate. We believe that EPA should identify the URTH levels and what constitutes "protective of public health".

We thank you for the opportunity to provide comments regarding this important matter.

Sincerely,

Ed Thomas

Electronic Attachments: 1. Rubin trade off health risk final.pdf

Response: See response to comment code 7000.

Commenter Name: James Talbot
Commenter Organization: Neverland Designs
EPA Document ID: EPA-HQ-OW-2009-0297-0456
EPA Comment ID: 28587
EPA Comment Code: 7000

Comment: Please put people above industry and keep our water pure

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0457
EPA Comment ID: 28588
EPA Comment Code: 7000

Comment: Keep our water clean, when it's gone, it's gone! It's very simple, no water = no life. Stop playing to big business.

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0513
EPA Comment ID: 28604
EPA Comment Code: 7000

Comment: Keep water clean!

Response: See response to comment code 7000.

Commenter Name: James Evangelos
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0548
EPA Comment ID: 28762
EPA Comment Code: 7000

Comment: To those in the EPA,

Why wouldn't you prevent this chemical from entering our waterways? How you could you think, that to some degree, this couldn't be harmful? Where are your standards? Frankly,would you want your own children exposed? Consider adopting a life of higher expectation; a life driven by the desire to do what is more difficult because IT IS THE RIGHT THING TO DO. The right thing to do hear is require perchlorate users responsible for the introduction into our water system to find a different way of disposing the chemical. Yes, that means money spent on research and development in order to create a manageable discarding mechanism. But is the alternative even thinkable: to expose our race to a chemical that could limit thyroid gland activity, ultimately leading to infant retardation, among a host of other unforeseen effects. I ask you to talk to your soul, deep down and see if it FEELS right to do what you are doing.

Kinldly , James Evangelos

Response: See response to comment code 7000.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0557
EPA Comment ID: 28765
EPA Comment Code: 7000

Comment: I am concerned about perchlorate in my drinking water. Please help keep it clean!

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0561
EPA Comment ID: 28768
EPA Comment Code: 7000

Comment: It doesn't suprise me that you think perchlorate is ok in drinking water when you think HsiF is ok despite your 7,000 EPA Uniion workers asking for a moratorium on it. Despite the fact that you have no safety documentation on this product. Despite the 3 plus year review of recent science on fluoride with it's conslusion saying fluoridation should cease. When will you do the job you are being paid to do? Does the word INTEGRITY mean anything to you? Does SCIENCE mean anything to you? You have proven that these words don't enter into the decisions you make.

Response: See response to comment code 7000.

Commenter Name: Robert Scrima Sr.
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0569
EPA Comment ID: 28771
EPA Comment Code: 7000

Comment: It is essential that our drinking water is healthy.Perchlorate is known to be very damaging especially to fetuses and young children. It has been shown to be very destructive to all humans.

In the past America maintained safe drinking water.The long term health costs to not doing so are enormous.The tragedy of illness caused by contaminates should be avoided at all costs.

Sincerely, Robert Scrima Sr. 727 Cassandra Lane Lakeland, FL 33809

Response: See response to comment code 6120.

Commenter Name: Peter Galvin
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0600
EPA Comment ID: 28778
EPA Comment Code: 7000

Comment: As a former federal regulator, I would like to urge you to keep the requirements and purpose of the law in mind in making your decision on this matter. Too frequently in recent years we have delayed or watered down necessary health actions because of fear of junk science submitted by impacted industries. Our counsel fall victim to fear of the lawsuit, and our leaderships fall victim to fear of individual congressional members responding to pressure from business organizations. The public has given you a mandate to protect water quality, and you should not hesitate to fulfill that expectation.

Peter Galvin

Response: See response to comment code 6120.

Commenter Name: Anonymous
Commenter Organization:
EPA Document ID: EPA-HQ-OW-2009-0297-0609
EPA Comment ID: 28780
EPA Comment Code: 7000

Comment: Mercury, perchlorate and raw sewage....what else? Why worry we will be under the Obama health plan!?

Response: See response to comment code 7000.

Commenter Name:
Commenter Organization: Seeds of Hope
EPA Document ID: EPA-HQ-OW-2009-0297-0632
EPA Comment ID: 28791
EPA Comment Code: 7000

Comment: Clean up the water-that's why we're using the healthcare system too much. We're sick because of contaminated water.

Response: See response to comment code 7000

EPA Comment Code: 7100 N/A May 2007 Comments

Response to Code 7100: Prior to publishing its preliminary regulatory determination for perchlorate (73 FR 60262, October 10, 2008) and its supplemental request for comment on the perchlorate regulatory determination (74 FR 41883, August 19, 2009), the Agency published a summary of the available information relevant to the perchlorate regulatory determination as part of its preliminary determination for 11 other contaminants on the second contaminant candidate list (72 FR 24016, May 1, 2007). EPA did not make a determination for perchlorate in the May, 2007 notice but rather described the available information relevant to the perchlorate regulatory determination and the steps the Agency planned to take to gather the information needed to make a regulatory determination. EPA received a number of comments related to perchlorate in response to this request. These comments are compiled in this section. See response to comment code 6120 for a discussion of EPA's decision to regulate perchlorate in drinking water. EPA's response to comments on the regulatory determinations for other contaminants under CCL 2 can be found at 73 FR 44251, July 30, 2008.

Individual Comments
Commenter Name: Marcia Willhite
Commenter Organization: Illinois Environmental Protection Agency
EPA Document ID: EPA-HQ-OW-2007-0068-0155
EPA Comment ID: 20256
EPA Comment Code: 7100

Comment: 217/785-478 May 23, 2007 Walter Docket Environmental Protection Agency Mailcode: 2822T 1200 Pennsylvania Ave, NW., Washington DC, 20460 Docket ID No: EPA--HQ--W--2007--0068

To Whom It May Concern:

Thank you for the opportunity to comment on the United States Environmental Protection Agency's ("Agency") Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List - Preliminary Determinations notice. In the notice it indicates that the Agency is seeking comment on 11 preliminary determinations. In addition, the notice stated:

While the Agency has not made a preliminary determination for perchlorate, this action provides an update on the Agency's evaluation of perchlorate. The Agency requests public comment on the information and the options that the Agency is considering in the evaluating Perchlorate and welcomes the submission of relevant, new information and/or data that may assist the Agency in its regulatory determination. (Emphasis added)

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Marcia Willhite
Commenter Organization: Illinois Environmental Protection Agency
EPA Document ID: EPA-HQ-OW-2007-0068-0155
EPA Comment ID: 20259
EPA Comment Code: 7100

Comment: Further, the two carcinogens, 2,4-dinitrotoluene, and 2,6-dinitrotoluene have been found in groundwater in numerous locations in Illinois, including Joliet Army Ammunition Plant at 10,000 µg/l, and Savanna Army Depot at 58.8 µg/l, respectively. These chemicals have caused, threatened, and allowed contamination of Class I: Potable Resource Groundwater in Illinois.

Thank you again for the opportunity to comment on this important matter. If you have any questions please contact Richard P. Cobb of my staff at the number referenced above.

Sincerely, Marcia Willhite,Chief Bureau of Water

Response: This comment is outside of the scope of this action, no response necessary. EPA's response to comments on the regulatory determinations for other contaminants under CCL 2 can be found at 73 FR 44251, July 30, 2008.

Commenter Name: Peter King
Commenter Organization: American Public Works Association (APWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0156
EPA Comment ID: 20260
EPA Comment Code: 7100

Comment: May 29, 2007 Water Docket US Environmental Protection Agency Mail Code 2822T 1200 Pennsylvania Avenue, NW Washington, DC 20460 DOCKET ID. NO: EPA-HQ-OW-2007-0068

Dear Assistant Administrator Grumbles:

The American Public Works Association (APWA) appreciates this opportunity to file comments on the proposed Regulatory Determinations Regarding Contaminants on the Seeond Drinking Water Contaminant Candidate List - Preliminary Determinations (72 FR 24016 (May 1, 2007)) and we agree with the decision announced in this notice. These comments were developed through input from APWA's Water Resources Management Committee.

APWA supports the Environmental Protection Agency's (EPA) efforts in making sound determinations as to whether or not a National Primary Drinking Water Regulation (NPDWR) should be developed for certain unregulated chemical contaminants under the Safe Drinking Water Act. The members of APWA's Resources Management Committee agree with the Agency's preliminary determination that a NPDWR is not appropriate for the eleven contaminants considered by EPA in this notice.

Response: No response is necessary to the information provided by the commenter. EPA's response to comments on the regulatory determinations for other contaminants under CCL 2 can be found at 73 FR 44251, July 30, 2008.

Commenter Name: Peter King
Commenter Organization: American Public Works Association (APWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0156
EPA Comment ID: 20262

EPA Comment Code: 7100

Comment: APWA represents 29,000 members who design, build, operate and maintain transportation, water supply, sewage and refuse disposal systems, public buildings, and other structures and facilities essential to the economy and way of life. Public works professionals serve a diverse range of local communities, municipalities, counties, townships, villages and districts, whether large or small, urban or rural. As stewards of public infrastructure, APWA members are dedicated to managing and operating water systems that provide safe and reliable service to their communities.

Please do not hesitate to contact APWA's Washington Office if we can be of help to you in the future.

Sincerely, Peter King Executive Director

Response: No response is necessary to the information provided by the commenter.

Commenter Name: Krista Clark
Commenter Organization: Association of California Water Agencies
EPA Document ID: EPA-HQ-OW-2007-0068-0157
EPA Comment ID: 20263
EPA Comment Code: 7100

Comment: June 11, 2007 Ms. Cynthia Dougherty Office of Groundwater and Drinking Water U.S. Environmental Protection Agency 1200 Pennsylvania Ave. NW Washington, DC 20460

Re: May 1st Federal Register Notice for Preliminary Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List (EPA-HQ-OW-2007-0068)

Dear Ms. Dougherty:

The Association of California Water Agencies (ACWA) would like to request an extension of the 60-day comment period on the May 1st Federal Register notice for the Preliminary Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List.

Response: See response to comment ID 20264 under comment code 7100.

Commenter Name: Krista Clark
Commenter Organization: Association of California Water Agencies
EPA Document ID: EPA-HQ-OW-2007-0068-0157
EPA Comment ID: 20264
EPA Comment Code: 7100

Comment: Our request for an extension to 120 days is driven by the complexity of the issues, including perchlorate, and the large volume of supplementary information not included in the

Federal Register notice that must be considered before any comments, if necessary, are submitted to the Agency.

Response: After careful review and consideration of the comments EPA received on the May 2007 notice, the Agency made a final determination in July of 2008 that no regulatory action was appropriate for any of the 11 CCL 2 contaminants. However, EPA has provided 2 opportunities for further comment on the perchlorate regulatory determination (please refer to the following Federal Register Notices: 73 FR 60262, October 10, 2008 and 74 FR 41883, August 19, 2009).

Commenter Name: Krista Clark
Commenter Organization: Association of California Water Agencies
EPA Document ID: EPA-HQ-OW-2007-0068-0157
EPA Comment ID: 20265
EPA Comment Code: 7100

Comment: ACWA believes the Contaminate Candidate List (CCL) is a critical element in developing drinking water standards. There are extensive policy and science issues involved in crafting and implementing this list, and as such, any related regulatory determinations should be thoroughly and carefully reviewed.

If you have any questions, do not hesitate to call me at 916-441-4545.

Sincerely, Krista Clark Director of Regulatory Affairs

Response: See response to comment ID 20264 under comment code 7100.

Commenter Name: Thomas Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0162
EPA Comment ID: 20266
EPA Comment Code: 7100

Comment: July 2, 2007 U.S. Environmental Protection Agency Office of Water Docket (Mailcode 2822T) 1200 Pennsylvania Ave. NW Washington, DC 20460

RE: Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List-Preliminary Determinations Docket EPA-HQ- OW-2007-0068

Dear Docket:

The American Water Works Association appreciates the opportunity to comment on the preliminary regulatory determinations from the second Contaminant Candidate List (CCL2) as detailed in the May 1st Federal Register notice (72 FR 24016). AWWA is an international, nonprofit, scientific and educational society dedicated to the improvement of drinking water quality and supply. Founded in 1881, the Association is the largest organization of water supply professionals in the world. Our 60,000 plus members represent the full spectrum of the drinking water community: treatment plant operators and managers, environmental advocates, engineers, scientists, academicians, and others who hold a genuine interest in water supply and public health. Our membership includes more than

4,700 utilities that supply roughly 80 percent of the nation's drinking water. Based on this broad membership base, these comments should be considered as representative of the drinking water community in general. These comments are divided into two major sections, starting with general comments, and then followed by comments on specific contaminants discussed in the May 1st Federal Register notice.

General Comments

As previously mentioned, AWWA appreciates the opportunity to comment on the above referenced preliminary regulatory determinations. The Contaminant Candidate List (CCL) and subsequent regulatory determinations are the foundation for the standardsetting process resulting from the 1996 Safe Drinking Water Act (SDWA) Amendments. These two components are among the most important changes in EPA's approach for developing national drinking water regulations since the SDWA was initially passed in 1974. Ensuring that the appropriate contaminant is selected for regulation is the critical first step in the development of national drinking water regulation that should subsequently be followed by setting the standard at the appropriate level for that contaminant.

The May 1st Federal Register address the preliminary regulatory determinations from CCL2 and the CCL process and the subsequent regulatory determinations are intertwined. AWWA has significant concerns with the parallel ongoing process for the third Contaminant Candidate List (CCL3) and those concerns will be sent in a separate letter to Cynthia Dougherty upon submission of these comments.

Section 1412(b)(1)(A) of the 1996 SDWA Amendments details the criteria for identification of contaminants for potential regulation:

i. the contaminant may have an adverse effect on the health of persons; ii. the contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and iii. in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

Another reform that is particularly applicable to this notice is found in Section 1412(b)(3)(A):

In carrying out this section, and, to the degree that an Agency action is based on science, the Administrator shall use -

(i) the best available, peer-reviewed science and supporting studies conducted in accordance with sound and objective scientific practices; and (ii) data collected by accepted methods or best available methods (if the reliability of the method and the nature of the decision justifies use of the data).

EPA's preliminary regulatory determinations for eleven contaminants on the second Contaminant Candidate List (CCL2) as published in the May 1st Federal Register complies with these two sections of the SDWA. AWWA commends EPA for not regulating contaminants purely for the sake of regulation, as was the case for some of the 83 contaminants listed in the 1986 SDWA Amendments. AWWA also commends EPA for using the best-available, peer-reviewed science in these preliminary determinations.

AWWA agrees with EPA's decision not to regulate these eleven contaminants. The occurrence levels are generally low based on national surveys such as the Unregulated Contaminant Monitoring Rule (UCMR), and regulation does not present an opportunity for significant risk reduction as mandated by the 1996 SDWA Amendments. These preliminary determinations follow the logic previously used in July 2003 for the first round of regulatory determinations and for the first six-year review (Roberson, 2005). AWWA believes that use of consistent logic in these two parallel regulatory efforts is important, contributing to a more transparent process, and commends EPA for proceeding in this manner. Based on the first round of regulatory determinations, a range of 0.02%-3.2% for national occurrence could be considered as the minimum threshold for development of a new regulation. National occurrence estimates for these eleven contaminants are well below this threshold, with boron having the highest prevalence of occurrence, at 1.7% of systems sampled in the National Inorganics and Radionuclides Survey (NIRS). Based on the first six-year review, a range of 0.53%-9.28% for national occurrence could be considered as the minimum threshold for revising an existing regulation.

Some might consider the lack of new contaminant regulations since the 1996 SDWA Amendments as an indication that this new regulatory development process is not working. AWWA disagrees with that viewpoint and believes, rather, that not regulating trivial contaminants is a positive development for EPA. Thirteen previously regulated contaminants had zero violations according to SDWIS data. Despite the lack of contaminant occurrence at levels of health concern, as inferred from the absence of violations for these contaminants, their regulation was nevertheless mandated by 1986 SDWA listing (Roberson, 2003).

A further indication that the new regulatory development process is working properly is the successful collection of occurrence data, through the Unregulated Contaminant Monitoring Rule (UCMR), to support regulatory determinations. Four of the contaminants (2,6-Dinitrotoluene, EPTC, Fonofos, Terbacil) in the current notice have zero occurrence based on the monitoring results from the first UCMR (UCRM1). These four contaminants were considered to be of potential concern based on the best information at the time back in 1998 when the first Contaminant Candidate List (CCL1) was published. UCMR1 monitoring results showed that these four contaminants were never detected in any of the more than 3,800 monitored systems.

AWWA recommends that EPA expand its discussion of the logic underlying the determinations for these eleven contaminants. The logic provided in the May 1st notice is not entirely clear. Generally, EPA needs to raise the level of transparency in its decision logic so that stakeholders can understand how data and information translate to determinations and to ensure consistency across the two parallel regulatory efforts (regulatory determinations and six-year review). For example, in the current notice there is no discussion about the remaining 40 CCL2 contaminants, what data are needed to make regulatory determinations, and what is being done to collect those data. Stakeholders have no way of knowing if more information on health effects or occurrence is required, or whether analytical methods research is needed before health effects and/or occurrence data can be reliably obtained.

The integration of EPA's overall drinking water research agenda with the overall regulatory development process is not sufficiently explained in this notice. The research being done on the balance of the contaminants from the second Contaminant Candidate List (CCL2) is not discussed. The process for conducting the appropriate research and then making the appropriate regulatory

decision for the 40 remaining contaminants needs to be clearly communicated to the drinking water community. For example, although national occurrence data from over 3,800 systems exists for acetochlor, molinate, and nitrobenzene, which were included in UCRM1 List 1, these three contaminants are not discussed at all in the May 1st Federal Register. It is unclear how the regulatory development process is driving EPA's research agenda.

AWWA recommends that, in the final notice, EPA develop a table on the information gaps for chemical contaminants similar to the table of pg. 24052 of the May 1st Federal Register for microbial contaminants. The limited research information in the current notice gives the appearance that little progress has been made since our 2002 comments on the first round of regulatory determinations. There is a strong need for appropriately communicating the body of research on CCL contaminants to the water sector.

AWWA wants to reiterate its concern that the 60-day comment period is not sufficient for adequately analyzing the complex issues surrounding perchlorate and for review, in general, of the associated background documentation. On May 22nd, AWWA requested an extension of the public comment period to 120 days and this extension was not granted. Not granting the requested extension is unfortunate, as the short comment period does not allow for adequate review by the drinking water community of the background documentation and for adequate debate on the complex policy issues. Perchlorate has been on EPA's regulatory agenda since its inclusion on the draft of the first CCL in 1997. While EPA has had over a decade to work through the complex policy issues surrounding perchlorate, the drinking water community had only 60 days to sift through these issues and make the appropriate policy decision.

Response: No response is necessary to the specific recommendations regarding transparency and information gaps as these comments were addressed in the July 2008 notice (73 FR 44255, July 30, 2008). Regarding the comment about perchlorate, please see response to comment ID 20264 under comment code 7100.

Commenter Name: Thomas Curtis
Commenter Organization: American Water Works Association (AWWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0162
EPA Comment ID: 20269
EPA Comment Code: 7100

Comment: Metolachlor

AWWA does not have any additional occurrence data on metolachlor or its degradates, but believes that more research is needed on the occurrence and health effects of many herbicides and pesticides and their degradates. The results of this research then need to be appropriately included in regulatory decisions by the Office of Pesticide Programs (OPP) and the Office of Groundwater and Drinking Water (OGWDW).

For example, metolachlor was not included in OPP's Cumulative Risk Assessment (CRA) for the chloroacetanilides because it was not apparent from currently available data that it shares the same target site in the nasal tissue as acetochlor, alachlor and butachlor, even though it does distribute to the nasal turbinates and "might" metabolize to quinoneimine, the active agent (as do acetochlor, alachlor and butachlor). Propachlor was also excluded from the Cumulative Risk Assessment for

similar reasons. EPA should promote further research to definitively determine whether or not metolachlor , a very widely used pesticide, is carcinogenic, as acetochlor, alachlor and metolachlor have very similar chemical structures.

The triazine herbicides are another example of the need to obtain the appropriate occurrence and health effects data of herbicides and pesticides and their degradates. AWWA has commented extensively in the past to OPP on the atrazine reregistration process. AWWA, through the Water Industry Technical Action Fund (WITAF) and a partnership with the Awwa Research Foundation (AwwaRF), has conducted extensive research on atrazine and its chlorinated metabolites. A listing of the published papers resulting from this research is enclosed as Appendix B.

The need for more occurrence and health effects data increases with the growing concern about potential reproductive and developmental effects from many herbicides and pesticides and their degradates. These new health endpoints will create monitoring and compliance challenges for water utilities, as the typical quarterly compliance monitoring is likely not appropriate for these new health endpoints. Both metolachlor and atrazine are on EPA's recently released draft list of 73 pesticides for Initial Tier 1 Screening as a potential endocrine disruptor under the Federal Food, Drug, and Cosmetic Act.

Methyl tertiary-butyl ether (MTBE)

AWWA supports EPA's decision not to make a regulatory determination for methyl tertiary-butyl ether (MTBE) at this time as the risk assessment is currently being revised. AWWA does not have any additional MTBE data to add to the topics listed in the May 1st Federal Register notice.

Microbial Contaminants

An information summary describing the state of the knowledge on the prevention, treatment, and health effects of cyanobacteria and its toxins would be useful for utilities and for state primacy agencies. The information should be concise and practical to ensure the document will be useful to water utility personnel. The summary should also include information on occurrence and conditions that might favor growth of algae and production of toxins. A strategy for communicating this information to utility customers should also be addressed. In addition to resources generated by EPA, the summary should include information of research funded by other organizations, particularly Awwa Research Foundation (AwwaRF).

Again, AWWA appreciates the opportunity to comment on these important drinking water issues. If you have any questions about these comments, please feel to call Alan Roberson or me in our Washington Office at 202-628-8303.

Yours Sincerely, Thomas W. Curtis Deputy Executive Director

cc: Ben Grumbles - USEPA OW Cynthia Dougherty - USEPA OGWDW Audrey Levine - USEPA ORD Brian Mannix - USEPA OPEI Alan Roberson Steve Via

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[APPENDIX A - see PDF] [APPENDIX B - see PDF]

Response: See response to comment ID 20264 under comment code 7100.

Commenter Name: Ed Thomas
Commenter Organization: National Rural Water Association (NRWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0163
EPA Comment ID: 20270
EPA Comment Code: 7100

Comment: July 2, 2007 U.S. Environmental Protection Agency Office of Water Docket (Mailcode 2822T) 1200 Pennsylvania Ave. NW Washington, DC 20460

RE: Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List-Preliminary Determinations (Docket Number: EPA- HQ-OW-2007-0068)

To Whom It May Concern:

NRWA commends EPA for it's caution in withholding regulatory action on the 11 contaminants reviewed to date under the second contaminant candidate listing process (CCL2) and concurs with EPA recommendations in this regard. NRWA's position concerning these 11 contaminants, as well as the remaining candidates on the list, is influenced primarily by two recent papers that bear directly on the occurrence data and the risk evaluations that are an integral part of the CCL review.

Response: See response to comment ID 20264 under comment code 7100.

Commenter Name: Diane VanDe Hei
Commenter Organization: Association of Metropolitan Water Agencies (AMWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0166
EPA Comment ID: 20274
EPA Comment Code: 7100

Comment: July 2, 2007 U.S. Environmental Protection Agency Office of Water Docket (Mailcode 2822T) 1200 Pennsylvania Ave. NW Washington, DC 20460

RE: Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List-Preliminary Determinations; Docket EPA-HQ-OW- 2007-0068

The Association of Metropolitan Water Agencies (AMWA) appreciates the opportunity to comment on the preliminary regulatory determinations for 11 contaminants as listed in the May 1, 2007 Federal Register (72 FR 24016). AMWA strongly supports the process required by the 1996 Amendments to the Safe Drinking Water Act (SDWA) that identifies potential contaminants, gathers needed information to determine if a national regulation is needed, and presents a formal evaluation and determination on whether or not to regulate a given contaminant.

Prior to the 1996 Amendments, Congress required regulation of specific contaminants based solely on the first step of the current process - the listing of potential contaminants. This lead to regulation of numerous contaminants that did not appear in drinking water at levels of public health concern

and wasted limited EPA and public resources. AMWA believes that this notice demonstrates that the 1996 process can work well in that the highest priority contaminants are selected for evaluation and that evaluation leads to informed decisions.

AMWA supports each of the 11 regulatory determinations made.

Response: See response to comment ID 20264 under comment code 7100.

Commenter Name: James Taft
Commenter Organization: Association of State Drinking Water Administrators (ASDWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0169
EPA Comment ID: 20284
EPA Comment Code: 7100

Comment: July 2, 2007 Comment Clerk Docket EPA-HQ-OW-2007-0068 Water Docket Environmental Protection Agency Mail Code: 2822T 1200 Pennsylvania Ave., NW. Washington, DC 2046 0

Dear Sir:

In response to the notice in the Federal Register of May 1, 2007 (Volume 72, Number 83) the Association of State Drinking Water Administrators (ASDWA) would is offering comments to the U.S. Environmental Protection Agency (EPA) on the Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant List -- Preliminary Determinations; Proposed Rule. ASDWA is the professional Association that represents the collective interests of the nation's state drinking water programs responsible for implementation of the Federal Safe Drinking Water Act.

Although some states have the expertise and resources to conduct their own evaluations of contaminant risk and may set their own, more stringent regulatory controls, most states rely on the EPA to determine which contaminants should be regulated in drinking water. It is critical that these determinations are based on sound science and accomplished through a transparent process with adequate input from all interested parties, especially the states. States expect EPA to follow the process prescribed in the Safe Drinking Water Act and we support the three statutory criteria for regulatory determinations:

(1) the contaminant may have an adverse effect on the health of persons;

(2) the contaminant is known to occur or there is substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and

(3) in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

ASDWA appreciates the opportunity to provide the perspective of states on EPA's preliminary determination of which contaminants from the second Contaminant Candidate List (CCL2) should be regulated. States are generally in favor of the regulatory decisions that EPA is proposing in this notice but we do have a few comments to offer.

States generally agree there is no significant occurrence nor any "meaningful opportunity for health risk reduction" in regulating the 11 contaminants EPA has preliminarily decided not to regulate. One state indicated that dacthal and its degradates did appear in some drinking water system monitoring in their state but that it could be effectively managed in the absence of a federal regulation. Therefore, ASDWA supports EPA's decision not to regulate the 11 contaminants on the list in the May 1, 2007 proposal.

Response: See response to comment ID 20264 under comment code 7100.

Commenter Name: James Taft
Commenter Organization: Association of State Drinking Water Administrators (ASDWA)
EPA Document ID: EPA-HQ-OW-2007-0068-0169
EPA Comment ID: 20288
EPA Comment Code: 7100

Comment: Metolachlor and Methyl tertiary-butyl-ether (MTBE):

As stated in the Federal Register notice, EPA's primary need here is for additional contaminant occurrence data to support its regulatory decisions. Monitoring conducted by water systems under UCMRI and coming under UCMR2 will provide a solid base of occurrence data for future determinations. Many states have assisted EPA in implementing the UCMR monitoring to help assure that systems monitor and report as required. We believe these new data will add significantly to EPA's knowledge of the occurrence of contaminants on the Contaminant Candidate Lists and others considered for regulation.

Thank you for your consideration of these comments. Please contact me at 703-812-9507 or jtaft@asdwa.org if we can provide additional information or if any clarification of these comments is needed.

Sincerely, James D. Taft Executive Director

Response: See response to comment ID 20264 under comment code 7100.

Appendix 1 – Complete List of EPA Comment Codes

Comment Code	Comment Topics	Comment Code Used?
1000	General Comments	Y
1100	SDWA requirements and the CCL and Regulatory Determinations process	Y
1200	EPA's handling in the October 2008 FR Notice of perchlorate-related comments that were submitted following the May 2007 RegDet2 FR Notice	N
1300	Length of the comment period following the October 2008 FR Notice	Y
1400	Supplemental Request for Comments	
1500	EPA's handling of comments on the October 2008 FR Notice	Y
1600	Length of the comment period following August 2009 FR Notice	Y
2000	Perchlorate Health Effects	Y
2100	NAS (NRC) review of perchlorate health effects and reference dose	Y
2110	Regulatory determination based upon the already-established RfD	Y
2150	EPA's decision not to seek further input from the NRC on issues related to perchlorate	Y
2200	Use of NHANES biomonitoring data for health effects evaluation	Y
2300	Use of PBPK models from Clewell et al (2007) and Merrill et al (2005) to evaluate health effects	Y
2400	Use of EPA's PBPK model to evaluate health effects	Y
2410	Use of PBPK model to select life-stage-specific HRLs	Y
2420	Suggestions for alternative ways to use the PBPK model to inform the regulatory determination	Y
2500	Other health effects studies, models, and data for EPA to consider (besides NAS/NRC report, NHANES biomonitoring data, and PBPK models already evaluated)	Y
2600	Comments on expanding scope of risk assessment to include other goitrogens and/or dietary iodide deficiency	Y
3000	Perchlorate Occurrence in Drinking Water	Y
3100	UCMR 1 occurrence analysis	Y
3110	UCMR 1 analytical methods and minimum reporting limits (MRL)	N
3120	UCMR 1 statistical methodology and nationally representative sample of small systems	Y
3130	UCMR 1 schedule and sampling plan	N
3140	UCMR 1 entry-point-level estimation of perchlorate exposure	Y
3150	Potential use of a Bayesian model to estimate number of PWSs and population served at a range of thresholds	Y
3160	Use of Census data to estimate populations that are in the sensitive life stage	Y
3170	Accounting for variation of perchlorate levels in public water systems over time	Y
3200	Supplemental drinking water occurrence data from California and Massachusetts	Y
3300	Other drinking water occurrence studies, models, and data for EPA to consider (besides UCMR 1 and California and Massachusetts data	Y

Comment Code	Comment Topics	Comment Code Used?
	already evaluated)	
4000	Evaluation of Perchlorate Exposure from Sources Other than Drinking Water	Y
4100	Dietary studies	N
4110	Dietary studies -- FDA's 2005-2006 total dietary study (TDS)	Y
4120	Dietary studies -- FDA's 2003-2005 exploratory survey data on perchlorate in food	N
4130	Dietary studies -- other studies, models, and data (besides FDA's 2005-2006 TDS, and 2003-2005 exploratory data)	Y
4200	Biomonitoring	N
4210	Biomonitoring -- urinary data from the 2001-2002 NHANES study, and EPA/CDC's NHANES-UCMR analysis	Y
4220	Biomonitoring -- breast milk studies discussed in the notice	Y
4230	Biomonitoring -- other biomonitoring studies, models, and data for EPA to consider (other than NHANES and breast milk studies discussed in the notice)	Y
4300	Other perchlorate exposure studies, models, and data for EPA to consider (other than drinking water, diet, and biomonitoring)	Y
5000	SDWA Criteria	Y
5100	SDWA Criterion #1 -- EPA's determination that perchlorate may have adverse effects on the health of persons	Y
5200	SDWA Criterion #2 -- EPA's determination that perchlorate occurs infrequently at levels of health concern in public water systems	Y
5210	Derivation of the RSC	Y
5220	Derivation of the HRL	Y
5225	Use of alternative HRLs specific to sensitive life stages, as described in Table 2 of the August 2009 FR notice.	Y
5230	Calculation of frequency of exposure above the HRL among pregnant women	Y
5240	Consideration of other sensitive subpopulations (e.g., infants, children, and persons with iodine deficiency or thyroid disorders) when establishing the HRL	Y
5300	SDWA Criterion #3 -- EPA's determination that regulating perchlorate with a NPDWR would not represent a meaningful opportunity to reduce health risks for persons served by public water systems	Y
6000	EPA Actions	Y
6100	EPA's preliminary determination not to regulate perchlorate	Y
6110	Comments urging EPA not to regulate perchlorate	Y
6120	Comments urging EPA to regulate perchlorate	Y
6125	Comments critical of preliminary determination (in the October 2008 FR Notice) specific to Washington Post article	Y
6130	Miscellaneous comments on the preliminary determination not to regulate (in the October 2008 FR Notice)	Y
6140	Additional new literature and information for EPA to consider when making a regulatory determination	Y
6200	Comments related to EPA's health advisory	Y
6210	Need for EPA to provide additional support to States and water systems	Y

Comment Code	Comment Topics	Comment Code Used?
6300	EPA's intention to revise guidance on clean-up levels (preliminary remediation goals)	Y
6310	Clean-up as a solution	Y
6400	EPA's decision to subject updated PBPK model to peer review during comment period (in the October 2008 FR Notice)	Y
6500	Comments on alternative risk reduction approaches	Y
7000	Miscellaneous Comments	Y
7100	N/A May 2007 Comments	Y

SUMMARY OF EXTERNAL PEER REVIEW COMMENTS AND DISPOSITION
for the 2008 external review draft of the report
Inhibition of the Sodium-Iodide Symporter by Perchlorate: An Evaluation of Lifestage Sensitivity Using Physiologically-based Pharmacokinetic (PBPK) Modeling

The draft report, *Inhibition of the Sodium-Iodide Symporter by Perchlorate: An Evaluation of Lifestage Sensitivity Using Physiologically-based Pharmacokinetic (PBPK) Modeling*, has undergone a formal external peer review performed by scientists in accordance with the U.S. EPA guidance on peer review (U.S. EPA, 2006). The external peer reviewers were tasked with providing written answers to general questions on the overall analysis and on parameter-specific questions in areas of scientific controversy or uncertainty. A summary of significant comments made by the external reviewers and the U.S. EPA's responses to these comments arranged by charge question follow. In many cases the comments of the individual reviewers have been synthesized and paraphrased.

The final external peer review report, including the charge to peer reviewers, (November 12, 2008) is available at http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=199347.

EXTERNAL PEER REVIEWER COMMENTS

The reviewers made several editorial suggestions to clarify specific portions of the text. These changes were incorporated in the document as appropriate and are not discussed further.

General Comments

Charge Question G1. ***Is EPA's analysis logical, clear and appropriate in depth and length? Has EPA accurately, clearly and objectively represented and synthesized the scientific evidence for the changes made to or specification of the model code and input parameters?***

Comment G1-a: All eight reviewers indicated that the U.S. EPA's analysis was logical, clear, and appropriate in length. Three reviewers explicitly indicated that the U.S. EPA provided an accurate, clear, and objective representation and synthesis of the scientific evidence for the changes made to or specification of the model code and input parameters. One reviewer recommended additional consideration and discussion of intra-human variability and quantitative and statistical approaches to address uncertainty.

> Response G1-a: In predicting perchlorate dosimetry and radioactive iodide uptake (RAIU) inhibition for the average individual in each lifestage, use of the model provides information for only a portion of the total human population variability. To characterize the full inter-individual variability within each lifestage would require specification of population distributions for each model parameter in each lifestage, including the distribution of sodium/iodide symporter (NIS) expression in each tissue where it occurs. Such data are not currently available. Further, the task of gathering all the requisite information, integrating it into a population parameter model (computer code), and

simulating the parameter distributions to estimate dose-response distributions is beyond the scope of the current effort.

Sweeney et al. (2003) is an example of using a physiologically-based pharmacokinetic (PBPK) model to evaluate overall population uncertainty, which is similar to what was suggested for perchlorate by the reviewer. Sweeney et al. (2003) performed an analysis for acrylonitrile (AN), where estimates of parameter variability were combined with model-prediction sensitivity coefficients (for each parameter) to estimate overall population uncertainty. Considering internal dose metrics of peak or average blood concentrations of AN or the key oxidative metabolite, cyanoethylene oxide, the ratio of exposure metric in the 99^{th} percentile of the population to the average individual was found to be no greater than 2.2. This is similar to the default inter-individual uncertainty factor for toxicokinetics of 3.

While the Sweeney et al. (2003) result is a single analysis, for a metabolized VOC, the intrinsic variability in human physiology incorporated by Sweeney et al. would be the same for perchlorate. However, to fully account for variability in the perchlorate analysis, one would also need to consider several additional factors across and within lifestages, such as variability in NIS levels and urinary clearance.

Comment G1-b: One reviewer noted that the draft report states that calculations were made for "subgroups, including potentially sensitive subgroups" although population-based modeling (with considerations of inter-individual and intra-individual variability) was not performed.

Response G1-b: A paragraph was added at the end of the introduction (Section 1) to clarify that the model predictions provided what could be considered central tendencies for specific subgroups.

Comment G1-c: One reviewer recommended considering the extent to which the gestation week 40 fetus may or may not represent the first and second trimester fetus.

Response G1-c: Text was added to the document (Section 4.2) to describe the rationale for using the model to predict %RAIU inhibition for only the gestation week (GW) 40 fetus. Briefly, the GW 40 fetus is not intended to represent the first or second trimester fetus. Key fetal parameters are too uncertain for quantitative application of the model to earlier GWs. There are no data to support model predictions of %RAIU inhibition in the fetus at the earlier GWs.

Comment G1-d: One reviewer asked for an expanded discussion of the motivation for some of the statistical fits to the data.

Response G1-d: Text was added to the beginning of Section 3 to provide a discussion and motivation for the methods used to estimate model parameters.

In short, the U.S. EPA's approach was to generate algebraic functions, through curve-fitting, that would provide good approximations of time- or BW-dependent changes in parameter behavior, using a relatively small number of parameters and simple

analytic tools (curve-fitting in Microsoft Excel) that could be readily applied. We believe that differences in the quantitative PBPK model predictions between using these curve-fits and what one might obtain by more extensive analyses would be small.

Charge Question G2. ***Please identify any additional studies or other data sources that should be considered in the assessment of the specific parameters addressed below, including urinary clearance (of iodide and/or perchlorate) and ingestion rates (breast milk, formula and water), especially in neonates.***

Comment G2-a: Five reviewers identified additional studies for the U.S. EPA to consider. One reviewer recommended that the U.S. EPA seek additional data to re-affirm the water ingestion rates, "particularly the use of the 90th percentile values in which the situations exceed the expectation of the fundamental knowledge." However, this reviewer was not aware of any studies or data sources that the U.S. EPA could use. One reviewer suggested that additional data collection could be done in the future, but noted that the U.S. EPA's use of DeWoskin and Thompson's data for scaling renal excretion for infants by body weight and extrapolating to a 60-day-old, 5 kg child is reasonable. One reviewer could not identify the reference Gentry et al. 2001 and suggested an alternative data source (Dewey et al., 1991) for the residual milk volume parameter.

Response G2-a: The Agency evaluated Dewey et al. (1991) and agrees that this reference provided a value (0.109 L) for residual milk volume that may be appropriate for use in the Clewell et al. (2007) model. Gentry et al. (2001) was referenced in the model code by the model authors for the original value used in the model (VMk = 0.632 L), but not in the corresponding manuscript and a Gentry et al. (2001) reference with this value could not be located. The value for residual milk volume (VMk) was changed from 0.632 to 0.109 L. Model sensitivity to VMk was tested and an 83% decrease from 0.632 to 0.109 L for VMk resulted in less than 3% change in model calculated percent inhibition of radioiodide uptake. Thus, the model is not sensitive to this parameter. This revision is documented in Appendix A, Section A.3, and an example of the impact of this change on model predictions is shown in A.7.

Comment G2-b: One reviewer recommended including a compartment analysis figure for the current model used by the U.S. EPA.

Response G2-b: Figures of the PBPK model structures, as they appeared in Merrill et al. (2005) and Clewell et al. (2007) for perchlorate and radioiodide were added to the report as Figures 1-1 and 1-2. Modifications to the model code did not alter the primary model structure shown in these figures, as originally published. However, the blood flow rates have been corrected to be blood plasma flow rates, rather than total blood flow rates, as described in detail in Appendix A, Section A.5.

Charge Question G3. ***Besides the specific parameters identified below, please comment on any other parameter or model choices described in the document that you think are incorrect or require further explanation or where other available information could provide better estimates.***

Comment G3-a: Two reviewers agreed with the U.S. EPA's parameter and model choices; one noted that the parameter values used by the U.S. EPA are supported by the literature. One reviewer stated that the methods used for scaling of clearance to body weight, age and surface area are appropriate; however, such scaling is most accurate when the substance is not reabsorbed or secreted. This reviewer recommended that the U.S. EPA consider alterations in NIS expression (Faggino et al., 2004) and whether other formulas could be used to more accurately reflect GFR in children and suggested two references (Check et al., 1977; Schrier, 2001). One reviewer declined to comment.

Response G3-a: The PBPK models were originally developed to simply describe the alterations in NIS expression for different lifestages. A change in NIS expression is assumed to be described by a change in the NIS maximum velocity (Vmax) which is scaled by $BW^{0.75}$. Using allometric scaling of Vmax, there is greater activity per tissue volume at a lower BW. Faggino et al. (2004) describes the use of immunohistochemistry to compare NIS (and Pendrin) expression in children less than 12 years to children greater than 12 years, and shows a higher percentage of stained cells in younger children (with intensity of staining ~ constant across age). In fact, this is what one expects/predicts from allometric scaling as currently used in the model: higher activity/tissue volume with lower BW. However, histochemistry only provides qualitative information. Also, because Faggino et al. (2004) only reported data for children in two categories (less than or greater than 12 years), the published results could not be used to evaluate the appropriate shape for an age-dependent function. The NIS expression data in Faggino et al. (2004) are not sufficiently detailed (vs. age or BW) to quantitatively inform the age-dependence of NIS.

The Agency also evaluated Cheek et al. (1977) for information to describe GFR in children. Cheek et al. (1977) indicates that creatinine serves as an indicator of tissue mass, and specifically, clearance would scale with muscle mass. The current PBPK model calculates muscle mass, as a constant fraction of body weight (BW). Therefore, to simply replace BW with muscle mass as the explanatory variable on which scaling is based would simply result in a change in the multiplicative constants with no change in the model predictions. Cheek et al. (1977) also states that intracellular water (ICW) correlates linearly with muscle mass, provides data on individual age, BW and ICW, and points to an earlier reference demonstrating that relationship. If the relationship is direct proportionality, then the results in Cheek et al. (1977) for ICW could be used directly to correlate muscle mass with age—age being the independent variable in the PBPK model. Otherwise (i.e., if the relationship includes a non-zero constant term), these data would need to be combined with those of the earlier paper to obtain the correct relationship for muscle mass vs. age, and clearance could be varied in proportion to muscle mass changes with age.

The general trend indicated – muscle mass increasing as a fraction of BW with age – means that scaling urinary clearance in proportion to muscle mass would lead to a prediction of *lower* clearance per unit BW in children of all ages, which would increase

the predicted dose-response (risk) relative to the current model application. The magnitude of this change cannot be determined without a complete data analysis but is likely to be most significant in younger children, where the difference in percent muscle mass is greatest. In addition, Clewell et al. (2002, Crit. Rev. Toxicol., 32:329-389), citing a physiology textbook, show a table with skeletal muscle increasing from 25% of BW in neonates to 40% in adults, which indicates that scaling urinary clearance with muscle mass would give results qualitatively in agreement with the current ones, though with a more mechanistic basis.

The reviewer also provided a reference on scaling clearance with creatinine levels, but use of such a formula would require a relationship between age or BW and creatinine levels. The pages in the Schrier (2001) reference noted by the reviewer are in a chapter by Clark and Chantler and describe the correlation of GFR with height and creatinine. Since Cheek et al. (1977) indicates that creatinine is an index for muscle mass, such an approach would likely lead to the same results as directly correlating clearance with muscle mass or ICW. So, there does not appear to be additional value in also evaluating an explicit correlation with creatinine levels. Therefore, while the U.S. EPA does not dispute the suggestion that scaling clearance with muscle mass is preferable in general, no such change has been made since the data or specific, quantitative information that would lead to substantive changes in model predictions for perchlorate and iodide are not available.

Comment G3-b: One of the reviewers stated the value used for the residual milk volume seemed unrealistically high and provided information and references for consideration. This reviewer recommended that the U.S. EPA conduct a sensitivity analysis to decide if and how this issue should be addressed.

Response G3-b: See response to comment G2-a. The residual milk volume parameter (VMk) was further evaluated by the U.S. EPA. VMk was changed from 0.632 to 0.109 L based on data from Dewey et al. (1991), as suggested by the reviewer, and is discussed in detail in Appendix A, Section A.3.

Comment G3-c: One reviewer noted that focused data collection might facilitate the improvement of the partition coefficient (PC) values used in the model as well as the urinary clearance values for perchlorate and iodide.

Response G3-c: Considering variation in PC values between species is usually modest, it is unlikely that age-dependent changes within a species (humans) will be large enough to substantially alter model predictions. The U.S. EPA agrees that additional data on the variation in perchlorate and iodide urinary clearance among humans would be valuable.

Comment G3-d: One reviewer requested that the rationale for using the 90^{th} percentile value be provided in the report. The reviewer noted that this value seems to be used as an upper bound limit, although the U.S. EPA states in the document that this is not the case.

Response G3-d: Additional rationale for using the 90th percentile value was added to Section 3.3 and 4.3. While the 90th percentile water ingestion rate characterizes a high-end drinking water exposure, the model prediction is not considered to be an 'upper-bound' because of the use of mean or average lifestage parameter values.

Comment G3-e: One reviewer stated that the U.S. EPA's analysis partially addressed biological susceptibility and coexposures; however, the Agency needs to consider additional susceptible subgroups (i.e., those with clinical and subclinical hypothyroidism, the genetically predisposed, and those that are iodine deficient) and the coexposures with thiocyanate and nitrate.

Response G3-e: The U.S. EPA's Office of Research and Development (ORD) was tasked with evaluating the effects of perchlorate on radioiodide uptake in different human lifestages using the Clewell et al. (2007) and Merrill et al. (2005) PBPK models and as noted by the reviewer, the U.S. EPA has accounted for perchlorate coexposure through both food and drinking water. Evaluating the impact of coexposure to other iodide uptake inhibitors (e.g. thiocyanate or nitrate) was not within the scope of this analysis.

Additionally, terms to account for co-exposures to thiocyanate and nitrate would have to be added to the models developed by Clewell, Merrill, and colleagues, and appropriately parameterized to represent their interactions with NIS. At a minimum such terms would have to include estimates of internal concentrations of these compounds and binding or inhibition constants for their interactions with NIS. This degree of model revision is beyond the scope of the current effort, and the data necessary to set the requisite model parameters may not even be available.

Likewise the models have not been specifically parameterized to describe hypothyroid or iodine deficient individuals. While the figure provided by the reviewer may in some ways be qualitatively correct, accounting for the impact of iodide deficiency would require a knowledge of the degree to which NIS levels change in the deficient person and also would require an understanding of the significance or impact of a change in iodide uptake. The current knowledge of thyroid function is insufficient to predict the impact of such incremental changes. Additionally, there are many factors (e.g. production and metabolism of thyroid hormones) that could affect iodide kinetics in a hypothyroid state, thus adjusting the PBPK models to accurately predict effects in hypothyroid/iodine deficient individuals would likely require an extensive amount of additional data collection, research and model development beyond the scope of this analysis.

The U.S. EPA's rationale for not evaluating these subgroups was added to the document in Section 5.1.

Comment G3-f: One reviewer identified a need to develop and thoroughly test a consistent framework for modeling [urinary clearance] processes for different lifestages. The reviewer stated that correcting the inconsistencies, identified in Appendix B of the document, would be a first step towards implementing such a framework.

Response G3-f: A more detailed response is provided under comment A1-e below (section on urinary clearance). The primary inconsistency identified by the U.S. EPA

was that urinary clearance of iodide and perchlorate were varied independently, sometimes quite differently, when the mechanism by which they are cleared is presumed to be the same. Based on that assumed common mechanism, the U.S. EPA concluded that when iodide clearance is decreased by 60%, for example, perchlorate clearance should also be reduced by 60%. The changes in the model implemented by the U.S. EPA corrected all such inconsistencies.

The significant physiological changes occurring in the mother at childbirth could result in a significant change in clearance between pregnancy and the postpartum period, so no further "consistency" in treatment of clearance across lifestages was assumed.

Charge Question G4. ***Please discuss research that you think would be likely to increase confidence in these models and their use in predicting RAIU inhibition by perchlorate in different life stages (for an average individual within each life-stage).***

Comment G4-a: Three reviewers provided recommendations for future research including assessing the effect of perchlorate on the clearance of NIS substrates, studying the mechanisms of perchlorate inhibition of NIS, investigating the toxicity of NIS substrates in the presence and absence of perchlorate, estimating urinary clearances of environmental pollutants in infants and neonates, biomonitoring of perchlorate, iodide, thiocyanate and thyroid hormone during and after pregnancy and during lactation in smoking and no-smoking women, measuring perchlorate in non-composited baby formula samples, and studying renal clearance of iodine and perchlorate during pregnancy and postpartum.

Response G4-a: The U.S. EPA agrees that additional information would be valuable to future revisions of the PBPK models.

Comment G4-b: Two reviewers recommended that the Agency consider additional methods. One suggested a probabilistic sensitivity/uncertainty analysis and eventually the feasibility of population-based PBPK modeling. The other reviewer asked the U.S. EPA to consider the possibility of simulating iodine-deficiency (or hypothyroidism) in pregnant women.

Response G4-b: The U.S. EPA recognizes that a powerful aspect of PBPK models is that they provide an excellent framework for parameterizing and simulating the effects of population distributions in physiological, biochemical, and metabolic parameters; however, this is outside the scope of the current analysis.

The reasons why the models were not extended to describe hypothyroid or iodine deficient individuals were outlined above in G3-e.

Comment G4-c: One reviewer noted that if model output is sensitive to the residual milk volume parameter (see questions G2 and G3), confidence in the modeling could be increased by a better description of this parameter. Another reviewer stated that using real-world data like those from Blount et al. (2006) with the model would increase confidence, but acknowledged that the Blount et al. study does not include children ages 6 and younger. Another reviewer recommended evaluating newer estimates of renal function by Schwartz.

Response G4-c: The PBPK model output for the lactating woman and breast-fed neonates were not sensitive to the residual milk volume parameter (VMk) value; however, the parameter value was changed to reflect the data in Dewey et al. (1991) (as explained in responses G2-a and G3-b and discussed in detail in Appendix A, Section A.3.).

Blount et al. (2006) provide data relating urinary levels of perchlorate to changes in T4 and TSH. Since the model does not predict T4 and TSH, these results could only be used qualitatively; i.e., if the urinary levels are converted to exposure rates, then the RAIU changes predicted over that range may be similarly significant. This would not provide significant support for the current analysis and was not explored further.

A paper for which Schwartz was the first author was not located; however, a recent publication by Work and Schwartz (2008) describes a clinical approach for measuring GFR in children, but it does not provide data that could be used to estimate values of GFR in children of different ages or BWs.

Comment G4-d: One reviewer recommended that the U.S. EPA state that the modeling effort is theoretical because it has not been validated; however, this reviewer suggested using existing data to help test the model predictions and validate the model. The reviewer noted that the U.S. EPA's report did not include information about concentrations of perchlorate and iodine in milk as a function of perchlorate dose and suggested reviewing Pearce et al. (2007) which provided the relevant information. The reviewer noted that without this information it is impossible to determine whether the U.S. EPA's results are consistent with the literature showing no correlation between perchlorate and iodine in breast milk samples.

Response G4-d: The model does predict inhibition of radioiodide transfer into breast milk, although those specific predictions were not included in the report. Pearce et al. (2007) showed no significant reduction (trend) in breast-milk iodide with perchlorate exposure, which is qualitatively in agreement with model-predictions, where inhibition of transfer to breast milk was found to be no more than a few percent – low enough to be insignificant relative the amount of variability in breast-milk iodide. The U.S. EPA plotted model predictions against the data of Pearce et al. (2007) to more clearly demonstrate the level of agreement between the two sets of results. This is now described in section 4.1.1.2 and shown in Figure 4-2 of the document.

Comment G4-e: One reviewer noted that the models use arterial plasma concentration and whole blood flow rates and recommends either the influx in all mass balance equations should correspond to whole blood concentrations or the flow rate should correspond to plasma flows. The reviewer suggested evaluating the assumption to see whether this change would have any consequence.

Response G4-e: As the reviewer suggested, plasma flow, instead of blood flow, should have been used to describe delivery of perchlorate and radioiodide to the tissues in conjunction with the concentration of perchlorate or radioiodide in the plasma. Cardiac output (total blood flow) was adjusted to reflect plasma flow by multiplying by the plasma:whole blood volume ratio (PBratio=Volume_of_Plasma / Volume_of_Blood =

~0.557), thereby decreasing the flow to the tissues. This had a minimal impact on model output within the experimental error for the average adult (at 7 μg/kg-day changed from 2.1% RAIU inhibition to 1.6%); however, the use of plasma flow was retained to increase physiological accuracy of the model. A description of this change was added to Appendix A, Section A.5.

Charge Question G5. ***Does EPA accurately characterize the strengths and limitations of the analysis? Please comment on any particular strengths that may not be mentioned or adequately characterized for the estimates of RAIU for different life stages. Please also comment on any specific sources of uncertainty that you believe have been overlooked in EPA's analysis or that require further discussion, and which might be significant to EPA's estimates of RAIU for different life stages.***

Comment G5-a: Four reviewers indicated that the U.S. EPA adequately characterized the strengths and limitations. One of these reviewers suggested that the U.S. EPA's modeling analysis could be improved by including comparisons of the model simulations to experimental data. Another reviewer agreed that the strengths and weaknesses of the analysis were adequately highlighted but noted that the limitations associated with the lack of validation were not addressed.

Response G5-a: Section 4.1.1 was added to include several comparisons of model predictions with published data.

Comment G5-b: Two reviewers did not specifically address whether the characterization of strengths and weaknesses was adequate. One reviewer identified the explicit listing of unresolved issues and inconsistencies in the modeling as the main strength of the analysis and description in the document. This reviewer listed the main limitations as the use of point estimates rather than a distributional approach to characterize exposures, the emphasis on "average" individuals rather than populations, and the lack of consideration of NIS inhibitors other than iodide and perchlorate. The other reviewer considered use of the PBPK model to assess life-stage sensitivity, use of the fetus to evaluate relative sensitivity, and consideration of relevant route/source of exposure as strengths of the analysis, whereas the exclusion of certain subgroups (e.g., the elderly, early gestation fetuses, iodine-deficient or hypothyroid pregnant women) and not considering parameter value variability within subgroups were weaknesses.

Response G5-b: The reviewers note observations about the limitations and weaknesses in the analysis of lifestage relative sensitivity of percent inhibition of thyroid radioiodide uptake using the Clewell et al. (2007) and Merrill et al. (2005) PBPK models. These observations and suggestions by the reviewers would provide for a strong population analysis, coexposure analysis, or analysis of other potentially sensitive subgroups (e.g. elderly, early gestation fetuses, iodine-deficient, or hypothyroid individuals). Incorporating these suggestions into the analysis would expand the scope of the lifestage comparison, but would not directly strengthen the current approach examining "average" individuals in the subgroups. Additional work beyond the scope of the current exercise and data collection would be necessary to improve upon the weaknesses mentioned by

the reviewers. For example, to accurately predict effects of perchlorate in populations exposed to other iodide uptake inhibitors would require additional PBPK models for the compounds of interest and additional data on the potential variability of parameters across populations would need to be obtained. Currently, urinary clearance is the only parameter for which we had sufficient data to test model sensitivity to several biological plausible values.

Comment G5-c: One reviewer recommended conducting an uncertainty analysis to look at the implications of using direct IV dose of radioiodide (rather than oral ingestion) for bottle-fed infants to determine iodide uptake inhibition.

Response G5-c: The models as developed by the authors were not intended to simulate the effect or to estimate the impact of perchlorate on inhibition of dietary iodide uptake, nor are the models capable of describing the large mass flux of dietary iodide. Additionally, the model developers (Clewell and Merrill) primarily used IV doses of radioiodide because the data in literature available on perchlorate's effect on thyroidal iodide uptake was predominantly from radioiodide given as an IV dose. This was maintained for all lifestages (except breast-fed infant) in this analysis to provide for determination of relative lifestage sensitivity. The Agency did not simulate an IV dose of radioiodide to the breast-fed infant, but rather accounted for the diminished amount of iodide the infant would receive through breast milk. This approach was used to also reflects a decrease in the external dose of iodide that a breast-fed infant would receive. For all other lifestages, perchlorate is assumed not to reduce the external dose of iodide.

Comment G5-d: One reviewer recommended additional discussion of the limitations of focusing on "healthy" individuals and of not considering large susceptible populations, and adding a scenario analyses to ascertain inhibition levels for plausible cases of higher susceptibility.

Response G5-d: A discussion of why the U.S. EPA focused on "average" or "healthy" individuals was added to Sections 5.1 and 5.2. Data are lacking to derive model parameters and validate model predictions of radioiodide uptake inhibition for individuals that may potentially be more susceptible. See response to G3-e for more detail regarding susceptible subpopulations.

Charge Question G6. ***As recommended in EPA's 2000 Risk Characterization Handbook, is the analysis transparent in terms of the steps, logic, key assumptions, limitations, and decisions? Specifically, does characterization of the results of EPA's work fully explain: a) the analysis approach employed; b) the use of assumptions and their impact on the analysis; c) the use of extrapolations and their impact on the analysis; d) plausible alternatives and the choices made among those alternatives; e) the impacts of one choice vs. another on the analysis; f) significant data gaps and their implications for the analysis; g) the scientific conclusions identified separately from default assumptions and policy decisions, if any; and h) the major conclusions, and the discussions of EPA's confidence and uncertainties in the conclusions?***

Comment G6-a: All reviewers agreed the analysis complied with the Risk Characterization Handbook and was transparent. Two reviewers recommended adding a separate section with a summary of the limitations and uncertainties, one of these reviewers also recommended adding lists of the data gaps and of the major perceived weaknesses. One reviewer recommended clearly listing plausible alternatives for some of the parameters and how these alternatives will affect the model.

> Response G6-a: A separate section (5.2) was added to the document that specifically addressed the limitations and uncertainties of the PBPK modeling. Alternatives and effects on model output for urinary clearance parameter estimates were listed in Table 4-2 of the document. No other alternatives were tested due to lack of information for possible alternatives.

Comment G6-b: One reviewer questioned the availability of additional data in the literature that could be used to further validate the model.

> Response G6-b: The U.S. EPA agrees that the existing data provide only limited potential for validation and additional data would be beneficial.

Comment G6-c: One reviewer stated that some of the justifications in the document are weak, especially with respect to inconsistencies in modeling urinary clearance processes. The reviewer acknowledged that correcting the inconsistencies may not substantively affect the calculated outcomes but a fully defensible model should incorporate up-to-date scientific information and assumptions that are consistent across lifestages.

> Response G6-c: As stated in responses above, the U.S. EPA identified and corrected inconsistencies in the treatment of urinary clearance, where possible. The U.S. EPA determined that the current approach is appropriately consistent with the assumed mechanisms and known differences in urinary clearance of perchlorate and iodide, and generally known changes in renal function across ages and lifestages.

Comment G6-d: One reviewer suggested clarifying why the elderly and teens were not included in the subgroups and why the results of the analysis are also applicable to chronic exposure situations. This reviewer recommended the U.S. EPA provide justification for the choice of 24-hr RAIU, and not 24-hr AUC (area under the plasma concentration versus time curve), as the endpoint and further discuss the sensitivity of key input parameters as a function of age to the use of a single RAIU value in infants and adults.

> Response G6-d: The NRC (2005) noted that fetuses, infants, and developing children are the most sensitive lifestages. When exposure from food and water is considered, infants and young children receive relatively higher doses than adults and fetuses. Thus, EPA chose to focus on these groups, as well pregnant and lactating women. Available data do not indicate that the elderly and teens are relatively more sensitive or highly exposed when compared with other lifestages. The results of this PBPK analysis are applicable to

chronic exposure situations because the perchlorate pharmacokinetics are such that steady-state is reached within a few days to a week. Longer-term changes in physiological variables associated with aging will result in changes in perchlorate pharmacokinetics, but those longer-term changed are largely bracketed by the specific ages and situations considered in this analysis. The National Academy of Sciences (NRC, 2005) concluded that if the perchlorate exposure is sufficiently low that the acute effect of RAIU inhibition is kept safely below the identified NOEL, then the risk of chronic exposure to perchlorate will be minimal. The U.S. EPA considers it unlikely that, at the levels of inhibition which occur at the RfD, there will be a cumulative long-term effect.

Justification for using 24-hr RAIU inhibition as the dose metric was added to the introduction (Section 1). Briefly, the series of PBPK models developed by Merrill and Clewell used RAIU inhibition as the primary dose metric. 24-hr RAIU inhibition was the dose metric chosen by EPA as opposed to a 24-hr AUC of perchlorate because the amount of RAIU inhibition was defined as a precursor to a critical effect and as the point of departure for the derivation of the RfD.

Comment G6-e: One reviewer recommended additional discussion on the forms for statistical fits, the use of 90th percentile versus mean values for parameters, the failure to address certain large susceptible populations, and the use of the GW 40 fetus. This reviewer requested more quantitative and rigorous treatment of uncertainty.

Response G6-e: Use of GW 40 fetus was described in G1-c response and text was added to the document in Section 4.2. The rationale for the use of 90th percentile for water ingestion was detailed in responses (G3-d, B1-d, C1-e, and C2-d) and additional rationale was added to Section 4.3 of the document. A discussion of other susceptible subgroups and the challenges in using the current PBPK models to evaluate these subgroups was added to Section 5.1 of the document.

Parameter-Specific Charge Questions

A. Urinary Clearance

Parameter-Specific Charge Question A1: ***Please comment on the appropriateness of the input values selected for maternal urinary clearance during pregnancy and lactation in EPA's analysis. Are the available data and rationale for the values selected transparently and objectively described? Are you aware of other publications or data that could be used to guide these choices or which provide alternative input values that are equally valid or more appropriate? Likewise, are the values selected for urinary clearance for the infant and older child the best estimates, given the available science and data? Are there other data that would provide better (or equally valid alternative) guidance or estimates? Is there any reason to believe that urinary clearance might not be a limiting factor in the elimination of perchlorate for infants?***

Comment A1-a: Regarding maternal urinary clearance, seven reviewers agreed that the input values were appropriate. The other reviewer disagreed with the rationale for the maternal

urinary clearance values but agreed with the value used for the lactating mother. This reviewer asserted that the available human data, which shows no measurable or consistent difference in urinary clearance between pregnant and non-pregnant women, should be used.

Response A1-a: The discussion of urinary clearance in the primary document has been expanded (Section 3.1) to more fully explain the U.S. EPA's rationale for selecting the urinary clearance rates used. Information is limited to derive maternal (during pregnancy and lactation) and infant clearance values; thus given the available information, the U.S. EPA believes the values used to be both appropriate for sensitive individuals and within the range of biological realism.

The available data and information are inconsistent and not clear to determine urinary clearance of perchlorate and iodide during pregnancy. General information on the clearance of metabolized compounds is considered a weak indicator for potential changes in iodide and perchlorate clearance because different mechanisms are involved.

Also, since clearance is the ratio of the urinary excretion rate to blood concentration, it is entirely possible for excretion to remain approximately constant, or even increase, while clearance is decreased. On average, excretion of iodide must equal its ingestion rate, independent of how clearance may vary. So, data in humans which show little or no changes in the clearance of other compounds, or little or no changes in iodide *excretion,* may still be consistent with a decrease in the urinary clearance of iodide and perchlorate. The PBPK modeling in rats, however, showed a decrease in the clearance of both perchlorate and iodide (both decreasing approximately the same amount).

Finally, while Aboul-Khair et al. (1964) measured iodide clearance directly, the methods used to measure blood iodide levels at that time were not the methods used to generate the more recent data available for rats. Thus the evidence for each of the three urinary clearance rate possibilities has both strengths and weaknesses, and the U.S. EPA concluded that none of the three was clearly superior. The U.S. EPA is not aware of newer data for urinary clearance of iodide or another entity with a similar clearance mechanism (e.g., bromate) that it could have used for pregnancy in humans.

Comment A1-b: Five reviewers specifically noted that the data and rationale were transparently and objectively described. One reviewer stated that the clearance rate choices for the mother during pregnancy and lactation were arbitrary and the rationale was not provided. One reviewer suggested the U.S. EPA improve the discussion of maternal urinary clearance values, and one reviewer also questioned the curve fit and data shown in Figure B-6.

Response A1-b: Additional explanation of the rationale for U.S. EPA's choice of maternal urinary clearance values has been added to Section 3.1. A general statement on the approach used for curve fitting was added to Section 3 (see response to comment G1-d) to address the reviewer's comment about Figure B-6.

Clewell et al. (2007) had estimated reduced urinary clearance of perchlorate during lactation (based on lactational rat:average adult differences) but assumed that iodide clearance was unchanged from the average adult. The U.S. EPA considers this option to be inconsistent, since changes in renal function that reduce perchlorate clearance are likely to have a similar effect on iodide clearance. Therefore this option

was not considered a plausible alternative for use during lactation. Further, the male rat PBPK model (Merrill et al., 2003) used urinary clearance rate (CLUC) values of 0.07 and 0.05 L/hr/kg$^{0.75}$, respectively, with virtually identical values in lactating rats (0.07 and 0.06 L/hr/kg$^{0.75}$, respectively; Clewell et al., 2003). Thus, the application of a "parallelogram" approach to extrapolate the rat results to humans indicates that clearance during human lactation should be the same as for the average adult (male) human, rather than having *both* perchlorate and iodide clearance reduced from the average adult, as was indicated during pregnancy. Therefore, the existing data support only two options for perchlorate and iodide clearance during lactation: increased clearance relative to the average adult, based on the results of Aboul-Khair et al. (1964) and equal clearance relative to the average adult, based on the PBPK modeling in rats. The U.S. EPA considers the two alternatives to have equivalent likelihood. Given this uncertainty, the U.S. EPA then chose the lower clearance (more sensitive) option: clearance equal to that of the average adult. Alternatives for clearance during lactation differ from pregnancy because the rat-based PBPK results do *not* indicate reduced clearance during lactation as they did for pregnancy; thus, reduced clearance during lactation was not considered for the lactating women subgroup.

Regarding Figure B-6, since use of the PBPK model versions for pregnancy and lactation involve integrating exposure and dosimetry over the weeks from conception and/or birth, it is helpful to use a smooth function with a simple form which captures the primary time-dependent changes in the various parameters, including clearance. The U.S. EPA decided that it would be efficient and reasonable to only consider simple, non-mechanistic functions, balancing the desire to capture the primary time-dependent changes against the potential problems in identifying parameters that can occur with more complex equations. A quadratic equation appears to satisfy these criteria appropriately, and the U.S. EPA does not believe that more meaningful information could have been extracted with an alternate function form.

It is not clear whether the apparent "dip" in clearance observed late in pregnancy (week 36 vs. weeks 32 and 38) is due to real changes in clearance or if it is due to experimental variability and measurement error. Consequently, without a supporting biological mechanism, the U.S. EPA considers the current model, which captures the long-term trend although not the shorter-term variation, to be appropriate.

The post-partum data in Figure B-6 are also taken from Aboul-Khair et al. (1964) – the same post-partum data shown in Figure B-5 just above. From the Aboul-Khair et al. (1964) data and figure, it appeared to the U.S. EPA that there is an overall downward trend in clearance starting around GW 30 and continuing through birth into the post-partum period. So, the data were included to guide the quadratic curve-fit to capture that trend.

It is clear to the U.S. EPA that increased iodide clearance during pregnancy is widely believed to occur, and the data of Aboul-Khair et al. (1964) are consistent with that assumption. However iodide clearance, per se, can only be determined by simultaneously measuring iodide blood levels and urine concentration or excretion rate in the same individual, and the literature search conducted by the U.S. EPA only identified the Aboul-Khair et al. (1964) paper with clearance data. However, the review of DeLange (2004) questions that assumption and instead suggests that clearance does not change during pregnancy.

While GFR may be related to cardiac output (QC) in general, it seems likely that it is the rate of kidney perfusion (QK) that is the actual determining factor. As currently formulated the model *QK does not change* during pregnancy. Increases in QC primarily serve the developing fetus, uterus, and breast tissues.

Comment A1-c: None of the reviews identified other publications or data; however, one reviewer recommended obtaining data on differences in urinary clearance data outside the perchlorate and iodide literature, and another reviewer suggested obtaining additional data to cross check assumptions regarding iodide uptake and renal clearance during pregnancy and early postpartum. No specific references were provided.

Response A1-c: The U.S. EPA agrees that changes in clearance of other substances would be informative, provided that such clearance was GFR-mediated or -determined. The U.S. EPA did seek to identify such data but no additional data were found, and therefore no additional data were included in the document. It is noted that data on clearance of pharmaceuticals is often proprietary and therefore not readily available in the open literature. Also, many if not most pharmaceuticals have rates of clearance that are determined by metabolism that would not be appropriate for extrapolating in this case.

Comment A1-d: With respect to urinary clearance rates for the infant and older child, six of the reviewers agreed with the values used and none of the reviewers disagreed or suggested alternative values. One reviewer referred U.S. EPA to alternative guidance for urinary clearance in neonates, infants, and children but did not find any evidence to contradict the assumptions used. Another reviewer noted that the estimates used for urinary clearance in infants and children reflect published GFR values. One reviewer recommended emphasizing inter-individual variability in the discussion and describing it quantitatively.

Response A1-d: It is clear that an explicit analysis of inter-individual variation would be informative. See response to G3-a for a discussion on possible alternate approaches to estimating clearance rates.

Comment A1-e: One reviewer identified inconsistencies to be clarified, particularly with respect to scaling, and areas for future research, e.g., a consistent treatment of the urinary clearance process for various life stages.

Response A1-e: The U.S. EPA's goal was to assure consistency in handling iodide and perchlorate clearance. A clarification was added to the beginning of Section 3. For example, when considering reduced clearance during lactation, if iodide clearance was reduced by 60% then the U.S. EPA also reduced perchlorate clearance by 60%. In this regard the U.S. EPA was indeed consistent in changing the perchlorate and iodide clearance parameters. However, Clewell et al. (2007) reduced perchlorate clearance during lactation 60% from the "average adult" value found by Merrill et al. (2005), but did *not* reduce iodide clearance. The U.S. EPA chose not to consider that option as it appears inconsistent.

On units of clearance, when simulating an individual the rate of urinary clearance of "x" is:

$$RAU_x \text{ (mg/hr)} = CLU_x \cdot CVK_x,$$

where the (scaled) clearance constant, CLU_x, has units of L/hr (equivalent to volume of blood cleared per time), and CVK_x is the concentration in the kidney venous blood and has units of mg/L. Thus the units of the clearance rate (RAU), clearance constant (CLU) and blood concentration are all consistent.

However, as is often the case in PBPK modeling, the clearance rate constant is assumed to scale allometrically, by $BW^{0.75}$, and is therefore defined as:

$$CLU_x \text{ (L/hr)} = CLUC_x \cdot BW^{0.75}.$$

In fact this equation defines $CLUC_x$ and in no way contradicts the physics of the problem, which is appropriately represented by the equation for RAU. Further, given the units of CLU as shown, and that BW has units of kg, it follows that the units of CLUC *must be* $L/h/kg^{0.75}$. Since the model code describes urinary clearance using these two equations, with $BW^{0.75}$ scaling, it follows that the listing of CLUC by Clewell et al. (2007) and Merrill et al. (2005) as having units of L/h/kg is a simple typographical error.

The U.S. EPA does not believe that the document will be improved by including this exposition, since the key points area already included, so no changes have been made.

Furthermore, the U.S. EPA considers use of $BW^{0.75}$ to be a good rule-of-thumb, both for scaling across species and among individuals within a species, in the absence of other data. However, very young children are not the same as small monkeys (despite euphemistic references) and even the data for basal metabolic rate variation across species shows scatter around the primary allometric relationship that cannot be completely described by a simple power function. Therefore species- or substance-specific data may well depart from this general relationship, and therefore we choose to use the more specific data over the generality when such data are available. The suggested paper by Johnson (2008) provides data which strongly indicate a departure from this scaling in neonates, which supports the use of clearance data in human children that departs from this relationship.

Regarding the "GFR-based scaling" in Figure B-2, this scaling is defined by equation B3, not B1 as the draft document erroneously indicated. The scaling involves a combination of scaling by $BW^{2/3}$ to approximate dependence on body surface area (SA) and a correction factor, the specific growth rate (SGR), to account for the fact that infant excretion falls below what one would predict based on SA alone, with SGR being a function of infant age. Since there is variation in individual BW at any given age, when this function is applied to a set of individual data with known ages and BW, the result is not a smooth function of age but reflects the variation in BW with age. Appendix B, Section B.3 has been modified slightly to correct this error and clarify these points.

Comment A1-f: One reviewer requested clarification on Figure B-4 and for the statement that the U.S. EPA considers its urinary clearance estimates in infants and children to be scientific estimates and not bounds.

Response A1-f: General statements have been added to the Introduction (section 1) to explain the reasons and approach for describing population average behavior, and details about the handling of urinary clearance also have been added to section 3.1. In addition, the text under Figure B-4 has been expanded to include further explanation.

If the normalized Lloyd et al. (1985) data (yellow diamonds in Figure B-4) are simply taken as a collection of values, assumed to be independent of BW, then one can estimate a mean, standard deviation, etc. The "Lower 95% of Lloyd et al.(1985) " line is simply a horizontal line plotted at a y-value equal to lower 95% confidence limit on the mean of the data. The data average line is likewise determined by combining the normalized Lloyd et al. (1985) and Chin et al. (1982) data, irrespective of BW, calculating the average of those values, and plotting a horizontal line with that value.

The primary point of this plot is to show that, while the normalized data (Clu/BW values) show some downward trend with BW, the error between the data and assuming BW^1 scaling, which corresponds to the horizontal line (when normalized to BW) is not substantially worse than using $BW^{2/3}$ or $BW^{0.75}$. There is not a strong BW-dependent trend in the data such that one of the later scaling curves better describes the data, and in fact those two curves substantially over-predict clearance for many of the individuals (data points) shown.

The scaling used by the U.S. EPA corresponds to the "~ Adult average" line in the plot. As shown, this scaling comes quite close to the data average and is above the 95% confidence limit on the mean of the Lloyd et al. (1985) data. Thus, it is considered an estimate of the population average, rather than a (lower) bound.

B. Breast-milk ingestion

Parameter-Specific Charge Question B1. **Infants are generally known to consume very little milk or formula on the first day of life, with ingestion quickly increasing over time. However the first time-point for which ingestion data are available for infants is at 7 days, which EPA extrapolated back to 0 ingestion at time=0 in its analysis (birth; Figure 1). The breast-milk ingestion rate was estimated based on mean values reported in Arcus-Arth et al. (2005), while the water ingestion used for the breast-feeding mother was the 90th percentile value from U.S. EPA (2004).**

Is EPA's extrapolation and rationale transparently and objectively described? Does this function appropriately characterize the available data and information? Are there other data that could be used to obtain a better or equally valid alternative estimate of mean breast-milk ingestion rate for infants in the first few days of life? Should an estimate other than the mean be used to determine the breast-milk ingestion rate?

Comment B1-a: None of the reviewers disagreed with the U.S. EPA's extrapolation. Five reviewers explicitly stated that the U.S. EPA's explanation was objective, and three noted that it was transparent. One reviewer pointed out that the modeling of perchlorate and iodine kinetics

in the neonate is highly uncertain, making this one of the weakest parts of the analysis. The reviewer recommended that this uncertainty be more clearly articulated in the document. One reviewer noted that the characterization would be confusing for readers that were not modelers.

> Response B1-a: Additional discussion of the uncertainty surrounding model predictions for neonates and fetuses was added to the document (Section 5.2). The reviewer is correct that modeling of perchlorate and iodine in the neonate is more uncertain than the adult. No data are available for the validation of the percent RAIU inhibition in the neonate or fetus. However, a small amount of data available for neonates was compared to model predictions of urinary radioiodide excretion (Clewell et al., 2007 – Figure 9). In the fetus, data were available to compare with model predictions of thyroid and blood radioiodide (Clewell et al., 2007 – Table 3) and serum perchlorate (Clewell et al., 2007 – Figure 10).

Comment B1-b: None of the reviewers disagreed with the use of the data in Arcus-Arth et al. (2005). One reviewer suggested that there are data in the literature for intake on days 1, 2, 3, 4, and 5, and that the values on days 4 and 5 are consistent with what was reported in Arcus-Arth, et al. However, no specific additional references were provided. Another reviewer asked that the decision to use Arcus-Arth et al. be clarified.

> Response B1-b: Further explanation on the use of Arcus-Arth et al. (2005) was added to Section 3.3.1. Data for days 1-5 (tabulated in Arcus-Arth et al., (2005) and originally reported in Casey et al., (1986)), in addition to other data for the first two months after birth, were used to derive the equation for the breast-milk ingestion rate. This approach is described in detail in Section 3.3.1 of the document. Data reported by Arcus-Arth et al. (2005) were chosen as the most complete and most recent data available that could be used to derive breast-milk ingestion rates and that included data for very young infants. The Arcus-Arth et al. (2005) study was designed to represent the infant population whose mothers follow the American Academy of Pediatrics (AAP) recommendations. It was a meta-analysis using data from various studies in the peer-reviewed literature, and intake was calculated on a body weight basis.

Comment B1-c: Two reviewers agreed with the extrapolation from day 7 to day 0, while three expressed questions or concerns about it. One reviewer stated that the extrapolation was not warranted because the newborn was not a subgroup used in the assessment of relative sensitivity of lifestages. The second questioned the abrupt increase in milk ingestion during day 1 and between days 1 and 7; however, that reviewer concluded that the mean breast-milk ingestion rate might be robust enough for use. Another reviewer stated that the use of body weight as a surrogate for age is illogical and recommended developing an expression for milk ingestion in terms of volume per body weight per day as a function of age. That expression could then be used to convert to the model parameter for the milk ingestion rate.

> Response B1-c: As a result of reviewer comments, the U.S. EPA has moved from using a power function to relate BW to breast-milk ingestion to using a Hill-function that describes breast-milk ingestion as a function of age. This change is shown in Section 3.3.

Briefly, while the newborn infant (< 7 days old) was not explicitly considered in this analysis, it is necessary to describe breast-milk ingestion the first 7 days of life as accurately as possible because the perchlorate ingested during this timeframe affects the %RAIU inhibition at 7 days of age, the neonate age that was first considered in this analysis. Additionally, the data tabulated in Arcus-Arth et al. (2005) for these few days after birth were first reported in Casey et al. (1986). Using these additional data, (now included in Figure 3-1), a Hill-function describing breast-milk ingestion rate (mL/hr) as a function of age (days) was derived and used in the PBPK model in place of the initial U.S. EPA power function relating BW (kg) to breast-milk ingestion (mL/hr). The Hill-function is a better predictor of the data, especially during the first 7 days after birth, than the table function originally implemented in the model by Clewell et al. (2007) and was easily implemented in the PBPK model code.

Comment B1-d: Two reviewers questioned the use of a mean value for infants and recommended further explanation of the rationale. One reviewer stated that using the 90th percentile for intake would lead to an unrealistically high estimate for milk consumption. Another reviewer thought that if the purpose was to determine the relative difference in iodide uptake inhibition for various subgroups, then the mean should be used consistently for all exposure and pharmacokinetic parameters throughout the analysis. Two reviewers recommended better accounting for variability. One noted that whether the mean should be used depends on steps later in the process and how variability is considered. This reviewer added that using mean values and the approach to computing the milk ingestion rate parameter precluded a fuller description of variability in iodide uptake inhibition. The other reviewer recommended using a distributional rather than a point calculation approach due to the large population above the 90th percentile and the potential "spread" of exposure factors above that percentile.

Response B1-d: The relative sensitivity analysis reported in Table 4-3 was conducted using a fixed dose-rate, 7 μg/kg-day, rather than any particular water ingestion value. The subsequent analysis (Table 4-5) where % RAIU inhibition is estimated for each lifestage does use upper percentile ingestion rates because the U.S. EPA's intent is to protect the entire population. However, as now stated in section 3.3 ("Post-natal PBPK Modeling") an average ingestion rate is used for breast-milk ingestion because in that case the neonate's exposure to perchlorate is due to the mother's ingestion, and an upper bound is used for the mother's ingestion. Assuming that the infant's ingestion of breast milk and the mother's ingestion of tap water vary independently, using an upper bound for both would be using a "double" upper bound for this lifestage alone, and therefore inconsistent with the bound used for other lifestages. Considering the breast-feeding mother and child as a unit, breast-milk ingestion may be thought of as an "internal" flow, for which the model represents the biological average rather than a distribution.

The U.S. EPA selected the 90th percentile drinking water intake value for most of the subpopulations evaluated in this report in order to explore the potential effects of high end exposure to perchlorate from public water systems. The approach is consistent with the Agency's *Guidelines for Exposure Assessment* (1992) and with the U.S. EPA policies and procedures for deriving health based drinking water values including Maximum Contaminant Level Goals (MCLG), Health Advisory values (HA), and Health Reference

Levels (HRL). The U.S. EPA acknowledges that modeling a complete distribution of water ingestion would be informative; however, due to time and data constraints the U.S. EPA selected a high-end exposure estimate as the most appropriate means to explore the potential effects of drinking water exposure on subpopulations.

The U.S. EPA does not believe that using mean drinking water intakes would characterize the high end exposures to perchlorate that may occur as a result of drinking water consumption. Similarly, the use values in excess of the 90^{th} percentile would be inconsistent with the Agency's policy to focus on realistic exposure scenarios and to avoid worst-case scenarios. The U.S. EPA further notes that less than one percent of public water systems reported detecting perchlorate at concentrations greater than 15 µg/L. Therefore, by evaluating populations consuming the 90^{th} percentile of drinking water with concentrations of perchlorate at 15, 20 and 24.5 µg/L, the U.S. EPA is providing a realistic high-end exposure estimate. See also the response to comment C1-c.

The primary points from this explanation have been added to Section 4.3.

C. Water ingestion

Parameter-Specific Charge Question C1. **For pregnancy, EPA used a normalized (90th percentile) water ingestion rate of 33 mL/kg-day (U.S. EPA 2004), which was multiplied by the maternal BW as described by the PBPK model growth-functions during pregnancy to obtain total water ingestion for the mother.**

Is EPA's approach and rationale transparently and objectively described? Is this approach appropriate for characterizing the upper-bound for ingestion of pregnant women? Are there other approaches or data that could be used to obtain a better or equally valid alternative estimate for this parameter? (Note that the self-reported body weight values in U.S. EPA (2004) indicate the same average body weight for pregnant women as for non-pregnant; data appears inaccurate, so the PBPK model body-weight description was used instead.)

Comment C1-a: Four reviewers agreed with the U.S. EPA's approach, and three reviewers explicitly stated that the approach was objectively described and transparent. One reviewer noted that the water ingestion was not extensively discussed and questioned if modifications were made to the variable in the Clewell et al. model. One reviewer stated that the U.S. EPA was inconsistent in choosing upper bounds or means for various parameters and thought that if the purpose was to determine the relative difference in iodide uptake inhibition for various subgroups, then the mean should be used consistently for all exposure and pharmacokinetic parameters throughout the analysis. One reviewer recommended a distributed zonal analysis rather than point calculations.

Response C1-a: See response to B1-d. Additionally, Clewell et al. (2007) did not describe water ingestion rates explicitly, but rather utilized constant dose rates (mg/kg-day), thus the water ingestion variables added by the U.S. EPA were new. As noted above and already clearly stated in the document, relative sensitivities were evaluated at a fixed dose-rate 7 µg/kg-day. Using such a fixed dose-rate provides a consistent basis for

evaluating relative sensitivity. The dose-rate might otherwise be calculated as the product of the water ingestion rate and water concentration, but for the relative sensitivity analysis it was set directly.

Comment C1-b: Four reviewers requested further explanation for how the 90th percentile value was derived and why it was used. Two of these reviewers recommended explaining why the 90th percentile value, rather than other values (such as the median or 95th percentile), was chosen for the computations.

Response C1-b: See response B1-d.

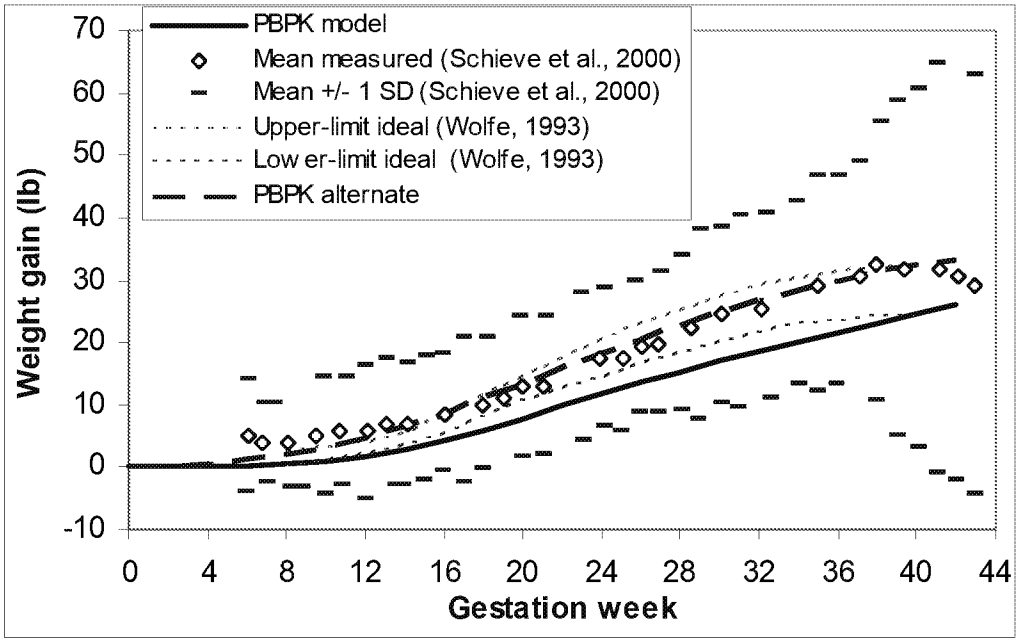
Comment C1-c: Two reviewers noted that the 90th percentile value was associated with a relatively small sample size (n = 65). One reviewer suggested this may be an underestimate and questioned the importance of the assumption and the sensitivity to the results. The other reviewer suggested using ingestion rates from Ershow et al. (1991), or to justify why they should not be used. This reviewer also questioned why the U.S. EPA specified total water ingestion rate but actually used the community water ingestion rate.

Response C1-c: The U.S. EPA selected community water ingestion for the analysis to characterize the high end exposure to perchlorate from public water systems (as opposed to bottled water or private well water which is captured in the total water ingestion). For a regulatory action under SDWA, the U.S. EPA's interest is in the impact of perchlorate in direct and indirect water. The reviewer is correct and this correction to the text has been made, as the analysis reflects that focus and that portion of water intake only. The U.S. EPA believes Kahn and Stralka (2008) and U.S. EPA (2004) are more recent and more appropriate data by which to evaluate the sensitive subpopulations of concern than is Ershow et al. (1991). The data from Ershow et al. (1991) were derived using data from the 1977-78 USDA Nationwide Food Consumption Survey, which is now 30 years old. . See also the response to B1-d.

Comment C1-d: One reviewer questioned the accuracy of the model growth-functions during pregnancy for estimating the body weight of pregnant women and suggested the U.S. EPA validate the weight estimates using NHANES data.

Response C1-d: While the CDC collects data on maternal weight gain and other health indicators for pregnancy, these appear to be just reported as total weight gain (from conception to just before birth), reported in the form of percent of population falling into various categories ("Under weight", "Normal weight," etc.), and do not include information on specific growth. However Schieve et al. (2000) reports BW gains during pregnancy from data for 3,511 mother-infant pairs from the 1988 National Maternal and Infant Health Survey, and Wolfe (1993) provides "upper-limit" and "lower-limit" values for ideal weight gain during pregnancy. Model-predicted BW gain is plotted against these published values below (the solid, dark-blue line is with the original model; the long-dashed, light-blue line is with PBPK model growth curves adjusted upward; the

mean and mean ± 1 SD are data from Schieve et al. (2000), and the "Upper/Lower-limit ideal" are from Wolfe (1993)).



Except for the apparent plateau in the data starting around GW 38, the shape of the model growth curve matches the observed growth curve quite well. While the curve falls somewhat below the observed mean (Schieve et al., 2000), it is well within one standard deviation of the mean, and since these were data not used in specifying the model, the agreement appears to be quite good.

Note that the data for the last few time points represent women who had not already given birth by that point; e.g., women who gave birth at GW 40 would not be included in the population represented at GW 42. So, the apparent plateau should not be construed as meaning that an individual woman's body weight would plateau or begin to decline in the last few GWs, but likely indicates that women who had the highest increase in BW by GW 38 (when the peak in the mean value occurs) gave birth in that week and so were not included in the population analyzed at later weeks. Since there is a tendency to induce labor before the child becomes too large to be safely delivered, the downward trend is then explained as a population shift, whereas the model growth-curve represents the change in a particular individual.

Finally, to test the sensitivity to BW, an alternate model version with the growth curve shifted upward was tested and compared to the original model. RAIU inhibition was evaluated at GW 40, given an exposure to 7 μg/kg-day (the POD). With the model as specified by the authors the RAIU inhibition predicted for the mother and fetus were 6.10 and 11.0%, respectively, and with the BW increased to better match the observed mean, the model predicted 6.14 and 11.1%, respectively. Thus the sensitivity of model predictions to changes in this range is negligible.

This information and figure were added to Section 4.1.1.1, Figure 4-1.

Comment C1-e: One reviewer recommended considering other approaches for estimating water ingestion for pregnant women. One suggestion was to consider water requirements for women in hot climates and choose a value somewhat above the 3.0 L/d considered an "adequate intake" by the Institute of Medicine (2004). The other suggestion was to pick a plausible upper bound from a cumulative distribution, and the reviewer offered that a value between 3.5 and 4 L/d seemed reasonable.

> Response C1-e: See response B1-d. The U.S. EPA recognizes that many women also drink bottled water and other beverages, for which any contribution to perchlorate exposure would be included in the "TDS" value. Thus the actual tap water ingestion is likely to represent only a fraction of the liquids ingested. Further, the U.S. EPA's objective is to estimate *actual* tap water ingestion in the U.S. population and the U.S. EPA believes the values currently used in the document are representative of the U.S. population exposure to tap water.

Parameter-Specific Charge Question C2. **For lactation, EPA used a fixed total (90th percentile) water ingestion rate of 2959 mL/day (U.S. EPA 2004), with the rationale that while the woman's weight and self-water demand are expected to drop after pregnancy (as described by the PBPK model time-dependent weight equations), the demand for milk production would be increasing, and the reported value was not for a specific age-range of child.**

Is EPA's approach and rationale transparently and objectively described? Is this an appropriate value to use for the ingestion rate of lactating women? Are there other better or equally valid alternative approaches or values that could be used?

Comment C2-a: Six reviewers agreed with the U.S. EPA's approach and five of these stated that the approach was transparent and adequately described. One reviewer requested clarification of the objectives of the analysis and reiterated that, if the purpose is to determine the relative difference in iodide uptake inhibition for different subgroups, then the mean should be used consistently for parameters throughout the analysis to avoid bias. One reviewer suggested that a probabilistic analysis would provide further insight and that a population/distribution-level analysis could be used to test the model in relation to data from Pearce et al. (2007) and Kirk et al. (2005, 2007).

> Response C2-a: The fixed ingestion rate of 7 μg/kg-day was used evaluating relative sensitivities, which is consistent in that the results show the differences in biological sensitivity, rather than differences due to changes in ingestion rates. As described in Response G1-a, sufficient data on NIS distributions that would be needed for a probabilistic analysis are not available at this time and the task of collecting and integrating the requisite information is beyond the scope of the current effort. The objectives of this analysis were elaborated upon in Section 1 of the document as well as

rationale for obtaining model predictions for the average individual, but using 90th percentile water ingestion, in each subgroup.

Comment C2-b: One reviewer questioned why the ingestion rate was substantially higher during lactation than pregnancy and recommended adding rationale for using a fixed ingestion rate. Another reviewer requested a better explanation for why a fixed ingestion rate was used, given the higher ingestion rate in lactating women on a mL/kg-day basis.

Response C2-b: As reported in Tables 6.3A-C in U.S. EPA (2004), the water ingestion rate of a lactating mother is greater than that of a non-pregnant or pregnant woman. This analysis reflects the recent data collected such that the water ingestion rate for the lactating woman (2.96 L/day) is greater than the non-pregnant (0.032 L/kg-day x 66kg = 2.11 L/day) and pregnant woman (0.033L/kg-day x 69-78kg = 2.18-2.57 L/day). Furthermore, instead of adjusting the lactating mother's water ingestion based on BW, which would decrease over time as the mother lost her weight gained during pregnancy, the water ingestion rate was kept constant. It is not known how the lactating mother's water ingestion changes over the first few months after giving birth. While it is possible that the mother's water ingestion may simply drop in proportion to her body weight, the U.S. EPA also considered the possibility that as the growing infant ingests an increasing volume of milk this would offset the reduced water consumption that would otherwise be expected to accompany a reduction in body weight. Therefore total water ingestion was kept constant, in the face of this uncertainty. This assumption leads to a higher predicted perchlorate dose, and hence effect, than if the mother's ingestion were assumed to decrease with her body weight.

Comment C2-c: Three reviewers questioned the use of the 90th percentile rather than the 95th percentile and asked for further explanation. One reviewer was concerned that a large number of mother-infant pairs are above the 90th percentile. Another reviewer suggested the U.S. EPA provide the rationale for selecting 2,959 mL/day at the 90th percentile and thought that providing the complete distribution of the water ingestion estimates would be helpful. The third reviewer asked why the U.S. EPA specified total water ingestion but used direct and indirect community water ingestion. This reviewer, noting the small sample size for the current value, also recommended using ingestion rates from Ershow et al. (1991), or justifying why they should not be used.

Response C2-c: See response B1-d.

Comment C2-d: One reviewer acknowledged that there are few data on the water needs of lactating women but presented the IOM (2004) argument that the intake of non-pregnant women added to the fluid output in breastfeeding provides a reality check on water ingestion rate. This reviewer recommended considering other approaches for estimating water ingestion for pregnant women. One suggestion was to consider water requirements for women in hot climates and choose a value somewhat above the 3.8 L/d considered an "adequate intake" by IOM (2004). The other suggestion was to pick a plausible upper bound from a cumulative distribution, and the reviewer offered that a value around 4 L/d seemed reasonable.

Response C2-d: See responses C1-e and B1-d.

The U.S. EPA seeks to identify a reasonable upper bound on tap-water consumption by women in the U.S. This ingestion rate may be less than an "adequate" intake, especially for women of warmer climates, since most of the U.S. has a moderate to cool climate and most people ingest beverages in addition to tap water to fulfill their water needs.

Breast-milk ingestion rises to an average of 25 ml/hr or 0.6 L/day in the first couple of weeks after birth, and continues rising to about 30 ml/hr or 0.72 L/day by 2 months. This is somewhat less than the exposure estimate change from 2.57 L/day for the GW 40 mother to 2.96 L/day for the lactating mother, but since a significant portion of breast milk will be lipids, an increase of 0.4 L/day appears appropriate.

Parameter-Specific Charge Question C3. **For bottle-fed infants, EPA made extrapolations of the 90th percentile water-ingestion in early life based on measurements made for the age ranges: 0-30 days, 1-3 months, and 6-12 months (points in Figure 2, upper panel). For the purposes of this analysis, bottle-fed implies feeding with formula requiring the addition of water.**

Is EPA's extrapolation and rationale transparently and objectively described? Does the overall function used to represent the changes in ingestion with age (and body weight) appropriately characterize the available data and information? Are there other data that could be used to obtain a better or equally valid alternative estimate of water ingestion rate for infants in the first few days of life (e.g., 7-day old)? The water ingestion rates used by EPA are based on 90th percentile ingestion data and thus are likely to exceed (minimal) physiological needs of infants as defined in nutritional guidelines. Are the water ingestion rates used by EPA reasonable in comparison to the physiological needs of infants at these various life stages? Are there other approaches or data (e.g., see the FDA memo) that could be used to obtain a better or equally valid alternative estimate for this parameter?

Comment C3-a: Seven reviewers agreed with the U.S. EPA's approach, and four of these reviewers stated that it was transparently and objectively described. One reviewer requested clarification of the objectives of the analysis and reiterated that, if the purpose is to determine the relative difference in iodide uptake inhibition for different subgroups, then the mean should be used consistently for parameters throughout the analysis to avoid bias. One reviewer noted that the reason for using a quadratic equation was not provided. Another reviewer stated that it was doubtful that using a single point estimate would provide an adequate understanding of the potential range of exposures and corresponding doses for bottle-fed infants.

Response C3-a: The fixed ingestion rate of 7 µg/kg-day was used for the relative sensitivity evaluation, thereby eliminating dependence on water ingestion for that calculation. Because data are not available for every age, it was necessary to fit a smooth curve to the data to predict water ingestion at the "in-between" ages. A quadratic equation was determined to provide an adequate fit to the data, consistent with the objective of performing a rapid and relatively simple analysis, and thus was used to estimate the ingestions at different ages. The U.S. EPA does not believe that using a 90th percentile ingestion rate provides an understanding of the range of potential effects from

different exposure scenarios, but rather characterizes the realistic, high-end exposure to perchlorate that may occur as a result of drinking water consumption.

Comment C3-b: One reviewer asked why the calculation was not scaled to 2 and 3 years and whether 0-7 days should represent another group or be removed (i.e., use 0-7 days or 7-30 days). Another reviewer questioned why the emphasis is placed on the section of the curve (i.e., the first few days after birth) that is not used in the lifestage analysis or supported by data.

Response C3-b: As stated in Response B1-c the first few days after birth are important in determining the infant's perchlorate concentration at day 7, and thus some estimate of intake must be used. Emphasis was not intended to be placed on the first 7 days following birth; however, it was necessary to make an estimate of ingestion during this timeframe. It did not seem logical to extrapolate the curve fit to data from Kahn and Stralka (2008) (shown in Figure 3-2A) such that the 1 day old infant consumes almost as much as the 7 day. Thus, the extrapolation was made back to 0, as shown in Figure 3-2B.

Additionally, a distinct set of computer files is used to simulate perchlorate dosimetry in older children (age 1 year and above), and dosimetry in older children is expected to have no dependence on exposures during infancy. Thus, the infant exposure calculation was not scaled to older children, and the two age ranges were analyzed separately.

Comment C3-c: One reviewer suggested that the U.S. EPA look at a report from a public health agency in Québec that has data on water ingestion rates for infants 8 weeks of age. One reviewer agreed that it was reasonable to use nutritional guidelines and that it would be useful to compare water consumption with what one would expect given nutritional guidelines and typical formula recipes, the nutritional guidelines would not lead to a reliable upper bound value for water consumption. None of the reviewers recommended using the approach outlined in the FDA memo as a better alternative to what was presented in the report.

Response C3-c: The values reported in a document published in Québec (Direction Risques biologiques, environnementaux et occupationnels, Institute national de santé, and Unité de recherché en santé publique, 2004) for bottle-fed only infants of 8 weeks (56 days) of age are slightly less than the values used by the U.S. EPA in this analysis. The 90^{th} percentile water ingestion values in the Québec report were 981 mL/day or 179 mL/kg-day for 8-week-old bottle-fed infants. The U.S. EPA did not estimate percent inhibition of radioiodide uptake for the 8-week old bottle-fed infant. These data provide support for the use of the 90^{th} percentile estimates from Kahn and Stralka (2008), but do not suggest a need to change the estimate for bottle-fed infants.

Comment C3-d: One reviewer recommended using nutritional guidelines to estimate the total water-ingestion rate. One reviewer offered an alternative approach for estimating ingestion rates for the first few days of life in which the data on breast milk consumption for the first few days (e.g., from Casey et al., 1986; Neubauer et al., 1993) are used. This reviewer suggested comparing literature values for breast milk consumption on days 1-7 to the values predicted for bottle-fed infants using the $1\text{-}e^{-day}$ function.

Response C3-d: Breast milk consumption for the first few days of life was tabulated in Arcus-Arth et al. (2005) from data reported by Casey et al. (1986). These data were considered in determining the breast milk ingestion rate for the breast-fed infants. Since individual ingestion can vary above or below nutritional guidelines and the U.S. EPA's goal was to estimate actual ingestion, the values from Kahn and Stalka (2008) were used in this analysis.

D. Perchlorate concentrations in formula

Parameter-Specific Charge Question D1. **EPA used 1.42 µg/L as the concentration of perchlorate in formula for bottle-fed infants. This estimate was based on information from FDA's Total Diet Study, supported by Pearce et al.'s (2007) findings.**

Is EPA's approach and rationale transparently and objectively described? Is 1.42 µg/L an appropriate value to use for the concentration of perchlorate in infant formula? Are there other better or equally valid alternative approaches or values that could be used?

Comment D1-a: Seven reviewers agreed with the U.S. EPA's approach, and five of these stated it was transparently and objectively described. One reviewer recommended adjusting the intake of perchlorate from infant formula to result in a daily exposure at the point of departure in order to provide results for a consistent comparison across all subgroups. Another reviewer recommended making the description more transparent and providing a sample calculation for Table 4 to show how perchlorate intake for bottle-fed infants was estimated.

Response D1-a: The bottle-fed infant formula contribution to perchlorate exposure was not set to result in a daily exposure equal to the point of departure (POD) because the concentration in infant formula should be reflective of the concentration in formula rather than the POD. The POD (7000 ng/kg-day or 7 µg/kg-day) was used in Table 4-3 for each lifestage to provide for a consistent comparison across lifestages. The FDA TDS data was added to the document and is shown in Table 4-4 along with the market basket averages and the overall average. A more detailed description of the calculation that yielded 1.42 ppb was added to Section 4.3.

Comment D1-b: One reviewer recommended that the U.S. EPA provide additional rationale for the selection of 1.42 µg/L, note in the document that the concentration values in Pearce et al. ranged from 0.2 to 4.1 ppb, and examine the sensitivity in uptake for a range rather than an average value. Another reviewer expressed concerns that the composite samples and detection limit (1 µg/L) of the FDA data do not provide an indication of higher end exposures. The reviewer also argued against using data on ready-to-eat formulas because the infants receiving that type of formula would not be part of the population drinking tap water. The reviewer recommended using either the highest value from the FDA study (3.6 µg/L) or a high value from the Pearce et al. (2007) study, based on measurements of undiluted (but intended to be diluted) formula (~3 µg/L). The reviewer added that better and more extensive measurements of perchlorate in infant formula are desirable.

Response D1-b: Additional rationale for the use of the 1.42 μg/L (ppb) from the FDA TDS study (Murray et al., 2008) was added to the document in Section 4.3. The U.S. EPA selected the Total Diet Study data (Murray et. al, 2008) to represent the dietary intake of perchlorate because TDS is the best available, nationally representative estimate of dietary exposure to perchlorate for the majority of the sensitive subpopulations of concern, including infants and children.

Model simulations were performed to examine the effect of using 1 ppb or 3.6 ppb (an upper end value from Pearce et al. (2007) instead of 1.42 ppb. Results of this sensitivity analysis were added to the document in Section 4.3.

The contribution of concern under SDWA is represented by the consumption of drinking water used to reconstitute powdered formula and formula concentrate. However, the U.S. EPA believes it is reasonable to compare the TDS data to an average value from Pearce et al. (2007) that included both ready-to-eat and concentrated formulas. After powdered formula is reconstituted with water, the concentration in the final product will be the sum of the amount in the powdered formula and that in the tap water. Since the perchlorate concentration in un-reconstituted powdered formula has not been reported, the U.S. EPA assumed that the contribution from the powdered formula after reconstitution (when the formula is ready for consumption) would be the same as the concentration in ready-to-eat formula. This is equivalent to assuming that ready-to-eat formula is made by reconstituting powdered formula with perchlorate-free water.

The U.S. EPA agrees that better and more extensive measurements of perchlorate in infant formula are desirable.

E. Radioiodide excretion into breast-milk by NIS

Parameter-Specific Charge Question E1. **In the model, EPA included perchlorate inhibition of NIS radioiodide excretion into breast milk, as well as inhibition of radioiodide transport by perchlorate for all NIS-containing tissues, thereby making the code consistent with the model description in Clewell et al. (2007).**

Is this inclusion appropriate? Are the impacts of this inclusion transparently and objectively described?

Comment E1-a: Seven reviewers agreed with the U.S. EPA's approach and stated that it was objectively and transparently described. One reviewer recommended reconsideration of Pearce et al. as these data do not suggest that there would be an effect of perchlorate on the excretion of iodine in breast milk; therefore, inclusion of this model feature may not be accurate. Another reviewer recommended adding a section towards the end that discusses the impacts of perchlorate inhibition.

Response E1-a: U.S. EPA is retaining in the model the perchlorate inhibition of radioiodide excretion in breast milk and believes it is consistent with the data in Pearce et al. (2007). The impact of including NIS inhibition of iodide transport into breast milk the model-predicted iodide concentration in breast milk by ~3% at a maternal dose equal to the point-of-departure (7 μg/kg-day). This small decrement is consistent with the

observations of Pearce et al. (2007), since the change is less than the variability seen in those samples. However, it should be noted that this reduction is essentially additive. That is, if the effect of the perchlorate alone on the infant is ~3% and the reduction in breast-milk iodide is ~3%, then the net effect on the amount of iodide taken up by the infant thyroid will be a ~6% reduction.

Published data have not shown a decrease in breast-milk iodide at low levels of perchlorate exposure. However, high-level perchlorate exposures (Kirk et al., 2005) and exposures to thyiocyanate (Laurberg et al. 2004) have been shown to decrease breast milk iodide. A full discussion of the impacts of perchlorate inhibition is beyond the scope of this document, but is available in the National Academy of Sciences review (NCR, 2005).

Comment E1-b: One reviewer noted that the rationale for scaling NIS levels to body weight was not clear and recommended review of studies (Faggino et al. and others) that suggest that scaling may not be appropriate as NIS expression changes over the course of development.

Response E1-b: See response to G3-a. U.S. EPA has reviewed the information recommended by the reviewer and has decided to retain the NIS scaling as originally described by the models' authors (Clewell et al. 2007 and Merrill et al. 2005).

Additional Reviewer Comments

Comment 1: One reviewer stated that the U.S. EPA should have considered easier and more straightforward approaches, e.g., Lorber (2008).

Response 1: While the Lorber (2008) model is able to predict perchlorate kinetics for the lactating woman and average adult, it was not developed to predict percent inhibition of radioiodide uptake by perchlorate and does not describe dosimetry in the pregnant mother, fetus, or child. Thus, the PBPK models by Clewell et al. (2007) and Merrill et al. (2005) were chosen to be the most appropriate tool for this analysis.

Comment 2: One reviewer noted that the water intake rates presented in Section 4.3 for 6- to 12-month olds and 1- to 2-year-olds do not appear logical or consistent with the values presented in Kahn and Stralka (2008). The reviewer recommended that they be checked.

Response 2: The reviewer is correct. The values were checked and found to be a typographical error. The values were corrected to reflect those from Table 4 of Kahn and Stralka (2008) that were used in the model.

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Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 2/2/2018 4:17:24 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
CC: Hafez, Ahmed [Hafez.Ahmed@epa.gov]
Subject: RE: Talking points on perchlorate peer review
Attachments: Perchlorate Peer Review Talking Points.docx

Hi Lisa,

Here is the requested input.

Thanks
Sam
==========
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Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Burneson, Eric
Sent: Friday, February 02, 2018 9:34 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Hafez, Ahmed <Hafez.Ahmed@epa.gov>
Subject: Talking points on perchlorate peer review

Jennifer has to speak with Lee this afternoon on the outcome of the perchlorate peer review. Can we draft short (not more than half a page) talking points with a high level summary of what we heard from the peer reviewers?

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Perchlorate - Independent Peer Review

- The Perchlorate Peer-Review public meeting took place on January 29 and 30, 2018. Eight panelists provided their feedback on the charge questions the agency charged them regarding the technical soundness of the scientific work developed by EPA.

- Panelists generally appeared impressed with the technical work developed by EPA as the scientific basis to help inform the regulatory decision for Perchlorate in drinking water.

- Stakeholders including: AWWA, Perchlorate Study Group (Via Intertox) and NRDC, provided public comments to the panel during the first day of the meeting.

- Several panelists made suggestions about improvements that could be made to both the BBDR Model and the MCGL approaches that might result in reducing uncertainties and incorporating new statistical metrics. Most panelists appeared to indicate that (based on the available science) the BBDR Modeling approach if far superior in predicting neurodevelopmental outcomes than the RfD approach.

Initial Feedback on BBDR Model:
- Panelists discussed the extent to which the BBDR model parameters should be incorporated into an uncertainty analysis.
- General agreement among panelists that the BBDR model is usable for the setting of an MCLG with moderate confidence in its performance.

Initial Feedback on Two-Stage Approach for informing MCLG:
- EPA has developed a 2-stage approach linking the revised BBDR model results with the quantitative information on neurodevelopmental outcomes from 5 epidemiological studies.
- General agreement among panelists that the second stage of the analysis requires additional consideration of the available data:
    - EPA should attempt to combine data (i.e. meta-analysis) from the positive 5 epidemiological studies if possible.
    - An evaluation of study quality (i.e. bias, sample size, etc.) should be applied to the 5 epi studies (and maybe the Group 2 studies too). This might result fewer studies being used in the stage-2 portion of the analysis.

Initial Feedback on Population-Based Approach for informing MCLG:
- Drs. Leung and Hattis don't like that an adverse cut-point needs to be defined for this approach as there is no such definition of adversity in the clinical setting.
- Dr. Roberts points out that the population-based approach avoids the uncertainties associated with the 5 second-stage epi studies.
- General agreement that this approach would support, but not replace, the 2-stage approach.

Next Steps:
- ORD/NCEA is developing a plan to describe how it intends to respond to the recommendations from the panelists and what is the time frame for completion.
- OGWDW is working with its contractor to outline a plan and schedule for completing necessary revisions to the Draft MCLG Approach Report.
- EPA expects the peer review panel to submit a final Peer Review report outlining all recommendations and responses to EPA's charge by early March.

Message

From: El Burai Felix, Alia [ElBuraiFelix.Alia@epa.gov]
Sent: 1/8/2018 3:20:21 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: High Level Summary - Perchlorate's Public Comments Matrix
Attachments: Summary of the Public Comments (01-08-2018).docx

Hi, Lisa!

Attached you can find the updated version of the High Level Summary of Perchlorate's Public Comments. Please let me know if you have any questions. Thank you!

Best regards,

Alia El Burai Félix, MS
Physical Scientist
U.S. Environmental Protection Agency (US EPA)
Office of Groundwater and Drinking Water (OGWDW)
Standards and Risk Management Division (SRMD)
Targeting and Analysis Branch (TAB)

Address: EPA East Bldg. Rm. 2357G
Office: 202-566-2572
Email: ElBuraiFelix.Alia@epa.gov

From: El Burai Felix, Alia
Sent: Monday, January 8, 2018 9:51 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: High Level Summary - Perchlorate's Public Comments Matrix

Hi, Lisa!

Thanks for your email. I will review your edits and make the appropriate changes to the document. Thanks in advance!

Best regards,

Alia El Burai Félix, MS
Physical Scientist
U.S. Environmental Protection Agency (US EPA)
Office of Groundwater and Drinking Water (OGWDW)
Standards and Risk Management Division (SRMD)
Targeting and Analysis Branch (TAB)

Address: EPA East Bldg. Rm. 2357G
Office: 202-566-2572
Email: ElBuraiFelix.Alia@epa.gov

From: Christ, Lisa
Sent: Thursday, January 4, 2018 1:35 PM
To: El Burai Felix, Alia <ElBuraiFelix.Alia@epa.gov>
Subject: RE: High Level Summary - Perchlorate's Public Comments Matrix

Hi Alia,
I had a few edits to the attached. Please review and make revisions as needed. I plan to go through this with Eric before the peer review meeting.
Thanks,
Lisa

From: El Burai Felix, Alia
Sent: Tuesday, December 19, 2017 3:31 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: High Level Summary - Perchlorate's Public Comments Matrix

Hi, Lisa!

Attached you can find the latest version of the High Level Summary of Perchlorate's Public Comments. I included the corrections we discussed in our meeting. Please let me know if you have any questions. Thank you!

Best regards,

Alia El Burai Félix, MS
Physical Scientist
U.S. Environmental Protection Agency (US EPA)
Office of Groundwater and Drinking Water (OGWDW)
Standards and Risk Management Division (SRMD)
Targeting and Analysis Branch (TAB)

Address: EPA East Bldg. Rm. 2357G
Office: 202-566-2572
Email: ElBuraiFelix.Alia@epa.gov

Message

From: El Burai Felix, Alia [ElBuraiFelix.Alia@epa.gov]
Sent: 12/19/2017 8:31:00 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: High Level Summary - Perchlorate's Public Comments Matrix
Attachments: Summary of the Public Comments (12-19-2017).docx

Hi, Lisa!

Attached you can find the latest version of the High Level Summary of Perchlorate's Public Comments. I included the corrections we discussed in our meeting. Please let me know if you have any questions. Thank you!

Best regards,

Alia El Burai Félix, MS
Physical Scientist
U.S. Environmental Protection Agency (US EPA)
Office of Groundwater and Drinking Water (OGWDW)
Standards and Risk Management Division (SRMD)
Targeting and Analysis Branch (TAB)

Address: EPA East Bldg. Rm. 2357G
Office: 202-566-2572
Email: ElBuraiFelix.Alia@epa.gov

Message

From: El Burai Felix, Alia [ElBuraiFelix.Alia@epa.gov]
Sent: 12/18/2017 2:24:14 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: High Level Summary - Perchlorate's Public Comments Matrix
Attachments: Summary of the Public Comments (12-15-2017).docx

Hi, Lisa!

Hope you had a good weekend. Attached you can find the High Level Summary of Perchlorate's Public Comments. We can discuss this further in our meeting at 9:30 a.m. Please let me know if you have any questions. Thanks in advance!

Best regards,

Alia El Burai Félix, MS
Physical Scientist
U.S. Environmental Protection Agency (US EPA)
Office of Groundwater and Drinking Water (OGWDW)
Standards and Risk Management Division (SRMD)
Targeting and Analysis Branch (TAB)

Address: EPA East Bldg. Rm. 2357G
Office: 202-566-2572
Email: ElBuraiFelix.Alia@epa.gov

Message

From: Georges, Jessica [Georges.Jessica@epa.gov]
Sent: 12/12/2017 12:57:52 PM
To: Hafez, Ahmed [Hafez.Ahmed@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
CC: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Public Comment Matrix
Attachments: WA459_T3_Public Comments Matrix_171208.xlsx

Good morning,

This email is just a reminder that I am still on the Perchlorate team.

I actually have not received any correspondence emails related to this team activities since Dan Olson's departure.

If I could be included on the meetings and email correspondences related to this team I would appreciate it.

Sincerely,
Jessica

From: Christ, Lisa
Sent: Monday, December 11, 2017 12:15 PM
To: Georges, Jessica <Georges.Jessica@epa.gov>
Subject: FW: Public Comment Matrix

Hi Jessica,
FYI –
Lisa

From: Hafez, Ahmed
Sent: Monday, December 11, 2017 9:59 AM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Miller, Gregory <Miller.Gregory@epa.gov>; El Burai Felix, Alia <ElBuraiFelix.Alia@epa.gov>; Helm, Erik <Helm.Erik@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: FW: Public Comment Matrix

Hello all,

Please find the attached comment matrix for the Perchlorate MLCG approaches Public Comments.

Let me know if you have any questions.

Thanks,
Ahmed

Ahmed M. Hafez, Ph.D.
OW/OGWDW/SRMD/TAB | Office: WJC East 2227Q
hafez.ahmed@epa.gov | phone: 202.564.1944

"The person you are the most afraid to contradict is yourself."
--N. N. Taleb

From: Lauren Brown [mailto:Lauren_Brown@abtassoc.com]
Sent: Friday, December 08, 2017 4:04 PM
To: Hafez, Ahmed <Hafez.Ahmed@epa.gov>
Cc: Lawrence Reichle <Lawrence_Reichle@abtassoc.com>; Ryan Klein <Ryan_Klein@abtassoc.com>
Subject: Public Comment Matrix

Hi Ahmed:
Attached is the most recent draft of all the public comments received. As with the ORD comments we've tried to underline the key comments and label the topic areas to allow for ease in sorting. We have some comments bolded as a carryover from what we did for ORD. However, we have not gone through this whole set of comments and bolded those that we believe are more important. If this is something you would like us to do please let us know, also let us know if there are any questions.

Thanks and have a nice weekend.
Lauren

Lauren Brown | Associate/Scientist | Abt Associates
O: 301.347.5832 | F: 301.828.9859 | www.abtassociates.com

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From: Lauren Brown
Sent: Wednesday, December 06, 2017 3:37 PM
To: Hafez, Ahmed (Hafez.Ahmed@epa.gov)
Cc: Lawrence Reichle; Ryan Klein (Ryan_Klein@abtassoc.com)
Subject: BBDR comments

Hi Ahmed:
Attached is the comment matrix we have pulled together for ORD. It includes all the comments we received related to the BBDR model. We've reviewed and **bolded** those that we believe are most important, though I think it would be best if ORD reviewed them all since they have a better understanding of the model and the implications of some of the comments. We have also taken your approach of trying to underline the most important part of the comment to help the reader.

In this matrix we have a "general topic" column which, for this spreadsheet, should almost all be the BBDR model as these were pulled from the larger matrix. We then have the "specific" topic area where one can drill down into the different areas that comments were received on. If you sort alphabetically by this column you should be able to easily group comments which are similar. We also kept in a column of some of our initial thoughts on some of the comments. These only pertain to comments for which we had quick initial responses to – this is has not been done systematically throughout the matrix.

Please let us know if you have questions on this.

Lauren

Lauren Brown | Associate/Scientist | Abt Associates
O: 301.347.5832 | F: 301.828.9859 | www.abtassociates.com

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Message

From: Hafez, Ahmed [Hafez.Ahmed@epa.gov]
Sent: 12/11/2017 2:59:14 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Miller, Gregory [Miller.Gregory@epa.gov]; El Burai Felix, Alia [ElBuraiFelix.Alia@epa.gov]; Helm, Erik [Helm.Erik@epa.gov]
CC: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Public Comment Matrix
Attachments: WA459_T3_Public Comments Matrix_171208.xlsx

Hello all,

Please find the attached comment matrix for the Perchlorate MLCG approaches Public Comments.

Let me know if you have any questions.

Thanks,
Ahmed

Ahmed M. Hafez, Ph.D.
OW/OGWDW/SRMD/TAB | Office: WJC East 2227Q
hafez.ahmed@epa.gov | phone: 202.564.1944

"The person you are the most afraid to contradict is yourself."
--N. N. Taleb

From: Lauren Brown [mailto:Lauren_Brown@abtassoc.com]
Sent: Friday, December 08, 2017 4:04 PM
To: Hafez, Ahmed <Hafez.Ahmed@epa.gov>
Cc: Lawrence Reichle <Lawrence_Reichle@abtassoc.com>; Ryan Klein <Ryan_Klein@abtassoc.com>
Subject: Public Comment Matrix

Hi Ahmed:
Attached is the most recent draft of all the public comments received. As with the ORD comments we've tried to underline the key comments and label the topic areas to allow for ease in sorting. We have some comments bolded as a carryover from what we did for ORD. However, we have not gone through this whole set of comments and bolded those that we believe are more important. If this is something you would like us to do please let us know, also let us know if there are any questions.

Thanks and have a nice weekend.
Lauren

Lauren Brown | Associate/Scientist | Abt Associates
O: 301.347.5832 | F: 301.828.9859 | www.abtassociates.com

From: Lauren Brown
Sent: Wednesday, December 06, 2017 3:37 PM
To: Hafez, Ahmed (Hafez.Ahmed@epa.gov)
Cc: Lawrence Reichle; Ryan Klein (Ryan_Klein@abtassoc.com)
Subject: BBDR comments

Hi Ahmed:
Attached is the comment matrix we have pulled together for ORD. It includes all the comments we received related to the BBDR model. We've reviewed and **bolded** those that we believe are most important, though I think it would be best if ORD reviewed them all since they have a better understanding of the model and the implications of some of the comments. We have also taken your approach of trying to underline the most important part of the comment to help the reader.

In this matrix we have a "general topic" column which, for this spreadsheet, should almost all be the BBDR model as these were pulled from the larger matrix. We then have the "specific" topic area where one can drill down into the different areas that comments were received on. If you sort alphabetically by this column you should be able to easily group comments which are similar. We also kept in a column of some of our initial thoughts on some of the comments. These only pertain to comments for which we had quick initial responses to – this is has not been done systematically throughout the matrix.

Please let us know if you have questions on this.

Lauren

Lauren Brown | Associate/Scientist | Abt Associates
O: 301.347.5832 | F: 301.828.9859 | www.abtassociates.com

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Message

From: Hafez, Ahmed [Hafez.Ahmed@epa.gov]
Sent: 10/19/2017 6:20:27 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
CC: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: RE: Call in information requested for Perchlorate Charge meeting

Hi Lisa,

I've contacted Versar and have the comments that were submitted to them to include comments from:

- PSG
- AMWA
- DoD
- Intertox
- The Chlorine Institute
- AWWA

I have SBA's comments. I'm unaware of any others from our Federal partners.

I've taken a first pass at the comments and have some thoughts. We can discuss it Monday or whenever is convenient.

Thanks,
Ahmed

Ahmed M. Hafez, Ph.D.
OW/OGWDW/SRMD/TAB | Office: WJC East 2227Q
hafez.ahmed@epa.gov | phone: 202.564.1944

"It is better to do things that you cannot explain, than to explain things that you cannot do."
--Nassim Taleb

From: Christ, Lisa
Sent: Thursday, October 19, 2017 9:02 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Hafez, Ahmed <Hafez.Ahmed@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: Re: Call in information requested for Perchlorate Charge meeting

All
Let's postpone the meeting until Monday to make sure we have the full set of comments on the charge.
Ahmed can you and/or Greg touch base with Versar to make sure they didn't receive comments we didn't see? There should be comments from DOD, PSG and NASA too
They may also be the in the docket

Thanks so much
Lisa

Sent from my iPhone

On Oct 19, 2017, at 8:36 AM, Burneson, Eric <Burneson.Eric@epa.gov> wrote:

At this point Ahmed I think that we just want you to have an opportunity to ask questions. However, I thought we had received more comments on the charge beyond those from SBA. I think there AWWA, DOD and PSG comments at least.

From: Hafez, Ahmed
Sent: Thursday, October 19, 2017 8:35 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: Call in information requested for Perchlorate Charge meeting

Good morning Eric,

I apologize for scheduling the meeting without being 100% certain of your availability (and over lunch time).

If it is all right, I would like to amend the invitation with your call in information.

I don't think there's much to discuss unless we received comments other than those from SBA which are the only ones I've seen. We do have a bit of time as the meeting with the Science Advisor is on the 26th, so please suggest a new date/time if one is more convenient to you.

Regards,
Ahmed

Ahmed M. Hafez, Ph.D. | Physical Scientist
Targeting and Analysis Branch | Standards and Risk Management Division
Office of Ground Water and Drinking Water | Office of Water
U.S. Environmental Protection Agency
1200 Pennsylvania Ave NW | Washington, DC 20460-0001
hafez.ahmed@epa.gov | phone: 202.564.1944 | fax: 202.564.3760
Office: WJC East 2227Q | Mail Stop: 4607M

"It is safer to accept any chance that offers itself, and extemporize a procedure to fit it, than to get a good plan matured, and wait for a chance of using it." -- Thomas Hardy

Message

From: Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]
Sent: 10/5/2017 3:25:38 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: FOR REVIEW: perchlorate extension letters
Attachments: AWWA Response Letter_cr-j.docx; PSG Response Letter_cr-j.docx; Chlorine Institute Response Letter_cr-j.docx; ACC Response Letter_cr-j.docx

Thanks for the opportunity to review. The attached documents include my edits.

From: Christ, Lisa
Sent: Thursday, October 05, 2017 9:09 AM
To: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Subject: FOR REVIEW: perchlorate extension letters

Hi Crystal,
Attached are response letters to requesters of comment extensions. Also attached are the incoming letters.
Let me know if you have questions, etc.
Lisa

Message

From: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Sent: 10/4/2017 2:48:02 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: Perchlorate public comment period extension requests - communicating informally to the organizations that requested an extension

Ok Will do.

From: Christ, Lisa
Sent: Wednesday, October 04, 2017 10:47 AM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: Perchlorate public comment period extension requests - communicating informally to the organizations that requested an extension

Can you please reply to all?

From: Hernandez-Quinones, Samuel
Sent: Wednesday, October 04, 2017 10:45 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: Perchlorate public comment period extension requests - communicating informally to the organizations that requested an extension

Hi Lisa,

There is a typo highlighted in the email below. The extended comment period now ends on November 20. It indicates November 30 in the note below.

Thanks
Sam

From: Christ, Lisa
Sent: Wednesday, October 04, 2017 10:42 AM
To: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>
Cc: Burneson, Eric <Burneson.Eric@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: Perchlorate public comment period extension requests - communicating informally to the organizations that requested an extension

Letters are attached

Requesters for extension of just the report comment period by 45 days:
AWWA – request to Mike Shapiro
American Chemistry Council – request to Sam Hernandez

- Thanks for your continued interest in perchlorate in drinking water
- You sent a letter requesting an extension of 45 days of the comment period for the draft report "Proposed Approaches to Inform the Derivation of a Maximum Contaminant Level Goal for Perchlorate in Drinking Water"
- I understand that the BBDR model revisions and analysis in the MCLG Aproaches Report represent complex analysis that require carfeul review.
- I believe that peer review is an important component of the scientific process to assure the use of the best available science, strengthen the interpretation of the reviewed material, and add credibility to the analysis.

- Although I'm not able to extend the public comment period by the full 45 days, EPA can extend it by 21 days – giving reviewers until November 30 to submit comments.
- I believe this will provide adequate time for review and comment while allowing EPA to work to meet deadlines established under the consent decree.

Requesters for extension of both comment periods; 45 days for peer reviewers and charge & 75 days for the report
PSG – request to Mike Shapiro
The Chlorine Institute – request to Sam Hernandez

- Thanks for your continued interest in perchlorate in drinking water
- You sent a letter requesting an extension of 75 days for the comment period for the draft report "Proposed Approaches to Inform the Derivation of a Maximum Contaminant Level Goal for Perchlorate in Drinking Water"
- Your letter also requested a 45 day extension of the public comment period for the draft list of peer reviewers and draft charge
- I understand that the BBDR model revisions and analysis in the MCLG Aproaches Report represent complex analysis that require carfeul review.
- I believe that peer review is an important component of the scientific process to assure the use of the best available science, strengthen the interpretation of the reviewed material, and add credibility to the analysis.
- Unfortunately EPA is not able to extend the comment period for the list of reviewers and the charge, stakeholders have had opportunity for input through the nominations process.
- I can extend the public comment period for the draft MCLG Approaches Report by 21 days.
- I believe this will provide adequate time for review and comment while allowing EPA to work to meet deadlines established under the consent decree.

From: Rodgers-Jenkins, Crystal
Sent: Wednesday, October 04, 2017 10:08 AM
To: Tiago, Joseph <Tiago.Joseph@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>
Subject: RE: Perchlorate public comment period extension requests - communicating informally to the organizations that requested an extension

On Sept 29th, Peter wrote to Mike (see email chain below)

First, we'll appreciate your input on whether we need to seek input from the AO on this approach as well. If we are good to move forward, we would communicate with the organizations that submitted the requests informally, then we'll need to draft formal response letters and quickly put together the FR notices that will be needed to modify the public comment periods. We'll certainly need your help to get these approved quickly.

I am checking in so that we can all be clear on who will informally communicate to the organizations about our response to their request. I am guessing the calls would need to happen this week. My understanding is that the FR notice went upstairs this morning and we expect the FR to be published next week.

I've asked Lisa to draft a few talking points in case Peter is planning to make the calls. We are fine with making the calls if Peter wishes to delegate to SRMD management.

Please let us know.

Take care,

Crystal

From: Burneson, Eric
Sent: Tuesday, October 03, 2017 8:06 AM
To: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: Fwd: Perchlorate public comment period extension requests

Crystal
I have not yet reviewed this notice. Can you please review and move forward as soon as Lisa gets this to you?
Thanks

Sent from my iPhone

Begin forwarded message:

> **From:** "Mclain, Jennifer" <Mclain.Jennifer@epa.gov>
> **Date:** October 2, 2017 at 1:43:46 PM EDT
> **To:** "Flaharty, Stephanie" <Flaharty.Stephanie@epa.gov>
> **Cc:** "Christ, Lisa" <Christ.Lisa@epa.gov>, "Huff, Lisa" <Huff.Lisa@epa.gov>, "Burneson, Eric" <Burneson.Eric@epa.gov>, "Tiago, Joseph" <Tiago.Joseph@epa.gov>, "Tricas, Marisa" <tricas.marisa@epa.gov>
> **Subject: Re: Perchlorate public comment period extension requests**
>
> Great. I will Lee know we are aiming for his review on Thursday.
>
> Jennifer
>
> On Oct 2, 2017, at 11:50 AM, Flaharty, Stephanie <Flaharty.Stephanie@epa.gov> wrote:
>
> > Thanks Lisa !
> >
> > **From:** Christ, Lisa
> > **Sent:** Monday, October 02, 2017 12:49 PM
> > **To:** Flaharty, Stephanie <Flaharty.Stephanie@epa.gov>; Mclain, Jennifer <Mclain.Jennifer@epa.gov>
> > **Cc:** Huff, Lisa <Huff.Lisa@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Tricas, Marisa <tricas.marisa@epa.gov>
> > **Subject:** RE: Perchlorate public comment period extension requests
> >
> > Hi Stephanie,
> > Sam already drafted a notice that I reviewed – he's getting OGC concurrence. He also drafted transmittal memos. WE should be circulating them for review soon.
> > Lisa
> >
> > **From:** Flaharty, Stephanie
> > **Sent:** Monday, October 02, 2017 12:40 PM
> > **To:** Mclain, Jennifer <Mclain.Jennifer@epa.gov>
> > **Cc:** Christ, Lisa <Christ.Lisa@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Tricas, Marisa <tricas.marisa@epa.gov>
> > **Subject:** FW: Perchlorate public comment period extension requests

Jennifer,

I have an FR template that we used for the last extension so I can draft the new notice. **Please let me know how much time we're are granting for the extension.**

Peter can sign the notice but we need to clear FRNs through OP prior to signature. Mike is out all week and Lee is in the office this Thursday and Friday. He is on travel all next week so this Thursday is our opportunity to have him send an email to clear the FRN through OP and higher. I'll need to end OW the draft FRN and action information sheet by Thursday morning and Macara will request that Lee clear it before he goes on travel next week.

Please let me know if you all can work with the timing.

Thanks,
Steph

Begin forwarded message:

> **From:** "Lousberg, Macara" <Lousberg.Macara@epa.gov>
> **Date:** October 2, 2017 at 10:51:50 AM EDT
> **To:** "Evalenko, Sandy" <Evalenko.Sandy@epa.gov>, "Nasir, Iqra" <nasir.iqra@epa.gov>
> **Cc:** "Ruf, Christine" <Ruf.Christine@epa.gov>
> **Subject: FW: Perchlorate public comment period extension requests**
>
> FYI, we'll be seeing an FRN shortly to extend the comment period on perchlorate.
>
> ---
>
> **From:** Campbell, Ann
> **Sent:** Monday, October 02, 2017 10:49 AM
> **To:** Lousberg, Macara <Lousberg.Macara@epa.gov>
> **Subject:** Fw: Perchlorate public comment period extension requests
>
> ---
>
> **From:** Forsgren, Lee
> **Sent:** Sunday, October 1, 2017 5:47 PM
> **To:** Mclain, Jennifer
> **Cc:** Shapiro, Mike; Grevatt, Peter; Campbell, Ann; Best-Wong, Benita; Burneson, Eric
> **Subject:** Re: Perchlorate public comment period extension requests
>
> Both Sarah and I concur and if you cc me on the FR package I will reach out it OP on the notice.

Sent from my iPhone

On Oct 1, 2017, at 11:37 AM, Mclain, Jennifer <Mclain.Jennifer@epa.gov> wrote:

> Thanks Mike. We plan to have the FRN and letter responses into review early this week.
>
> Jennifer
>
> On Oct 1, 2017, at 11:32 AM, Shapiro, Mike <Shapiro.Mike@epa.gov> wrote:
>
> > I think you should proceed, given the timing. We will probably need an affirming note from Lee, but since he has already concurred that shouldn't be an issue.
> >
> > Mike
> >
> > Michael Shapiro
> > Deputy Assistant Administrator
> > US EPA, Office of Water
> >
> > On Sep 29, 2017, at 11:36 AM, Grevatt, Peter <Grevatt.Peter@epa.gov> wrote:
> >
> > > First, we'll appreciate your input on whether we need to seek input from the AO on this approach as well. If we are good to move forward, we would communicate with the organizations that submitted the requests informally, then we'll need to draft formal response letters and quickly put together the FR notices that will be needed to modify the public comment

periods. We'll certainly need your help to get these approved quickly.

From: Shapiro, Mike
Sent: Friday, September 29, 2017 11:19 AM
To: Grevatt, Peter <Grevatt.Peter@epa.gov>; Mclain, Jennifer <Mclain.Jennifer@epa.gov>
Cc: Campbell, Ann <Campbell.Ann@epa.gov>; Best-Wong, Benita <Best-Wong.Benita@epa.gov>
Subject: FW: Perchlorate public comment period extension requests

Jennifer and Peter,

Both Lee and I are on board with your recommendations on the Perchlorate extension requests. What's the next step?

Mike

Michael Shapiro

Acting Assistant
Administrator,
Office of Water

US EPA, 4101M

1200 Pennsylvania
Ave., NW

Washington,
DC 20460

202-564-5700

From: Forsgren, Lee
Sent: Friday, September 29, 2017 7:09 AM
To: Shapiro, Mike <Shapiro.Mike@epa.gov>
Subject: Re: Perchlorate public comment period extension requests

Mike

Those are parameters that I talked about with them so I would agree as well.

Lee

Sent from my iPhone

On Sep 28, 2017, at 11:24 PM, Shapiro, Mike

<Shapiro.Mike@epa.gov> wrote:

Lee,

I'm supportive of the OGWDW recommendation, which is no extension for the comment period on the charge and panel members and 21 day extension for the comment period on the report. This is the most we can do without further delaying our

schedule, which is already extremely challenging.

Mike

Michael Shapiro

Acting Assistant Administrator, Office of Water

US EPA, 4101 M

1200 Pennsylvania Ave., NW

Washington, DC 20460

202-564-5700

From: Mclain, Jennifer
Sent: Thursday, September 28, 2017 1:07 PM
To: Forsgren, Lee <Forsgren.Lee@epa.gov>
Cc: Shapiro, Mike <Shapiro.Mike@epa.gov>; Best-Wong, Benita <Best-Wong.Benita@epa.gov>; Grevatt, Peter <Grevatt.Peter@epa.gov>; Burneson, Eric

<Burneson.Eric@epa.gov>; Campbell, Ann <Campbell.Ann@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Tricas, Marisa <tricas.marisa@epa.gov>; Drinkard, Andrea <Drinkard.Andrea@epa.gov>

Subject: Perchlorate public comment period extension requests

Lee,

As discussed, here is a paper providing potential options for EPA's response to extension requests on the perchlorate peer review materials.

Please let me know if you would like to discuss further or if you have any questions. We are also working on communications for an

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Message

From: Tricas, Marisa [tricas.marisa@epa.gov]
Sent: 9/6/2017 4:38:48 PM
To: Drinkard, Andrea [Drinkard.Andrea@epa.gov]; Dennis, Allison [Dennis.Allison@epa.gov]
CC: Mclain, Jennifer [Mclain.Jennifer@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]; Tiago, Joseph [Tiago.Joseph@epa.gov]
Subject: Final Communications Roll-Out Plan
Attachments: Perchlorate Peer Review Roll Out_09.06.17.Finalv2.docx

Hi Andrea and Allison,

Attached you will find the Final Communications Roll-Out Plan for the Perchlorate Peer Review.

Sincerely,

Marisa Tricas
Communications Specialist
Office of Ground Water and Drinking Water
United States Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington, D.C. 20004
Office: 202-564-2955
Mobile: 202-770-5092
Office: WJC East 2104D
Website: https://www.epa.gov/ground-water-and-drinking-water

Perchlorate Peer Review
Communications Plan

PUBLICATION RELEASE DATE: September 11, 2017

ACTION: The agency is undertaking an independent, external panel peer review and announces the release of scientific materials for public comment that will inform the Safe Drinking Water Act decision making on perchlorate. **KEY MESSAGES**

- Perchlorate – a chemical used in rocket propellants and other applications – may disrupt the normal function of the thyroid gland in both children and adults.
- EPA is currently determining the appropriate scientific approach for understanding the health impacts of exposure to perchlorate in drinking water.
- EPA is conducting a peer review of the draft scientific approach to provide advice to EPA on steps that will yield a highly credible scientific product that is supported by the scientific community.
- EPA will use this peer reviewed science to make future decisions on perchlorate under the Safe Drinking Water Act.
- The agency is releasing the interim list of peer review candidates, draft charge questions as well as a draft scientific report.
- The report provides information regarding how EPA intends to apply BBDR model to inform a quantitative understanding of potential adverse health effects associated with exposure to perchlorate in drinking water.
- The scientific analysis is precedent-setting, therefore EPA is conducting a transparent and rigorous expert peer review process.
- After the peer review is complete, EPA will take the next appropriate steps.

ANTICIPATED REACTION

There is likely to be considerable interest and response to EPA's release of peer review materials and the peer review process itself. Over the past several years, stakeholders have provided extensive comments on publically reviewable perchlorate materials and notices, met with EPA senior officials, managers and staff and have written the Administrator numerous letters.

EPA was sued by NRDC for the Agency's failure to issue proposed and final regulatory actions for perchlorate in accordance with the timelines provided in SDWA. The court approved consent decree established a schedule for completing the peer review process (10/18/17) and signature of a proposed (10/31/18) and final rule (12/19/19).

Stakeholders and the press are aware that EPA has been working to implement SAB recommendations and develop a BBDR model and scientific approach to inform decisions on perchlorate.

Stakeholder response will generally be critical of the highly technical, underlying science to model perchlorate in sensitive lifestages and the novel application of the model output to inform an understanding of the health impacts of exposure to perchlorate in drinking water.

- Industry groups (Perchlorate Study Group, American Chemistry Council); drinking water utilities, the U.S. Chamber of Commerce and the Department of Defense will likely be critical of the underlying science
- Environmental groups will likely be critical of the underlying science.
- Consumers, both those using public water systems and private wells, will be concerned about potential health risks from perchlorate.

Perchlorate Peer Review
Communications Plan

DESK STATEMENT

Ensuring the safety of drinking water for all Americans is a top priority for EPA. The agency has initiated a peer review and is releasing scientific materials that inform decision making on perchlorate under the Safe Drinking Water Act. The materials include an interim list of peer review candidates, draft charge questions as well as a detailed report describing the biologically based dose-response model EPA developed and information regarding how EPA intends to apply modeling to understand the health impacts of exposure to perchlorate in drinking water. After the peer review is complete, EPA will take the next appropriate steps on perchlorate under the Safe Drinking Water Act.

Background

On January 8, 2009, EPA released an interim drinking water health advisory of 15 parts of perchlorate for every billion parts of water (parts per billion or ppb). This level was determined using a reference based dose response based on the recommendation of the National Research Council (NRC).

In 2011, EPA announced its decision (76 FR 7762) to regulate perchlorate under the Safe Drinking Water Act (SDWA). In accordance with SDWA, the Agency requested EPA's Science Advisory Board (SAB) to review how to consider available data in deriving a Maximum Contaminant Level Goal (MCLG) for use in developing a perchlorate National Primary Drinking Water Regulation. The MCLG is a non-enforceable goal defined under the SDWA as "the level at which no known or anticipated adverse effects on the health of persons occur and which allows an adequate margin of safety." The MCLG is one of the considerations in developing the enforceable maximum contaminant level (MCL) for a regulated contaminant. The SAB released its final report on May 29, 2013 and recommended that EPA "derive a perchlorate MCLG that addresses sensitive life stages through physiologically-based pharmacokinetic/pharmacodynamic (PBPK/PD) modeling."

In response to the Science Advisory Board's recommendations, the Office of Water worked with scientists from the Office of Research and Development and the Food and Drug Administration to develop a biologically based dose-response (BBDR) model that accounts for population differences in iodide exposure and predicts changes in thyroid hormone levels that result from exposure to perchlorate. We also assessed epidemiology studies that link thyroid hormone changes to developmental effects. EPA completeda peer review of the BBDR model and the report provided by the reviewers can be found on EPA's website at:
https://www.epa.gov/dwstandardsregulations/perchlorate-drinking-water.

Legal Deadlines: On February 18, 2016, the Natural Resource Defense Council filed a complaint for the Southern District of N.Y., alleging that EPA failed to perform a nondiscretionary duty under SDWA to propose and finalize a national primary drinking water regulation for perchlorate. On October 18, 2016, the court approved a consent decree establishing dates for –

- completing the peer review process (10/18/17, non-enforceable);
- filing a peer review status report (10/30/17); and
- signature of a proposed and final rule (10/31/18 and 12/19/19, respectively).

Perchlorate Peer Review
Communications Plan

COMMUNICATIONS MATERIALS

Webpage (link will appear on https://www.epa.gov/dwstandardsregulations/perchlorate) will include:

- Link to public inspection FR notice
- Draft Charge Questions
- Interim List of Peer Reviewers
- Draft scientific report on the application of the model to inform decisions on perchlorate

RELEASE SCHEDULE

-3 days

- OGWDW/SRMD notification of Regional Contacts
- OPA notification of Regional PADS

-2 days

- SRMD notification of federal partners (FDA, ATSDR, NIEHS, OMB)
- OPA calls to federal agencies' communications

Release Day (when publically available on FR site)

9:00 a.m	Begin head's up calls to stakeholder list below
10:00 a.m	Congressional heads up emails
12:00 p.m	Website goes live – Broader congressional notifications (emails with link to website).
1:00 p.m	Social media and stakeholder notification via email (Water Headlines listserv)

STAKEHOLDER NOTIFICATION

OGWDW:

- Michael Deane, Director, National Association of Water Companies
- Tracy Mehan, Government Affairs Director, American Water Works Association
- Mike Paque, Executive Director, Groundwater Protection Council
- Alan Roberson, Executive Director, Association of State Drinking Water Administrators
- Lynn Thorp, National Campaigns Director, Clean Water Action
- Diane Van de Hei, Executive Director, Association of Metropolitan Water Agencies
- Sam Wade, Executive Director, National Rural Water Association
- Nathan Ohle, Executive Director, Rural Community Assistance Partnership
- Tom Neltner, Chemicals Policy Director, Environmental Defense Fund
- Alexandra Dapolito Dunn, The Environmental Council of States

OGC:

- Eric Olson/Mae Wu, Natural Resources Defense Council

OLEM (OSRTI):

- Association of State and Territorial Solid Waste Management Officials

Perchlorate Peer Review
Communications Plan

EXTERNAL QUESTIONS AND ANSWERS

CONSUMER QUESTIONS

Where is perchlorate found?
Perchlorate occurs naturally in arid states in the Southwest United States, in nitrate fertilizer deposits in Chile, and in potash ore in the United States and Canada. It also forms naturally in the atmosphere. Perchlorate is manufactured and used as an industrial chemical and can be found in rocket propellant, explosives, fireworks and road flares. It has been found in some public drinking water systems and in food.

Why is perchlorate in drinking water a health concern?
Perchlorate may disrupt the normal function of the thyroid gland in both children and adults. In adults, the thyroid plays an important role in metabolism, making and storing hormones that help regulate the heart rate, blood pressure, body temperature, and the rate at which food is converted into energy. In fetuses and infants, thyroid hormones are critical for normal growth and development of the central nervous system. Perchlorate can interfere with the human body's ability to absorb iodine into the thyroid gland which is a critical element in the production of thyroid hormones.

How does perchlorate get into my drinking water?
Perchlorate is dissolves easily, is relatively stable and is mobile in water. While it has often been detected in water supplies in close proximity to sites where solid rocket fuel is manufactured or used, there are also many locations in the United States lacking a clearly defined source.

Besides drinking water, how else can people be exposed to perchlorate?
People are exposed to perchlorate primarily through eating contaminated food or drinking water. The Food and Drug Administration (FDA) Total Diet Study combines nationwide sampling and analysis of hundreds of food items along with national surveys of food intake to develop comprehensive dietary exposure estimates for a variety of demographic groups in the U.S. In the 2008-2012 survey the FDA found detectable levels of perchlorate in 97 percent of the foods sampled. The complete set of FDA perchlorate data can be found here:
[HYPERLINK "https://www.fda.gov/Food/FoodborneIllnessContaminants/ChemicalContaminants/ucm077615.htm"]

Have public drinking water systems been sampled for perchlorate?
Customers served by a public water system can contact their local water supplier and ask if they test for perchlorate. If so, they are encouraged to obtain a copy of their Consumer Confidence Report. This report lists the levels of contaminants that have been detected in the water, including those tested by EPA, and whether the system meets state standards or guidelines. If you are concerned about the possibility of perchlorate in your drinking water and you are served by a private well, EPA recommends testing your drinking water. In addition, EPA recommends that residents reach out to their local public health department for more information on testing your water.

The most recent Consumer Confidence Report can be obtained from your drinking water utility, by visiting their website or contacting them for a copy. Some public water systems upload their Consumer

Confidence Report to EPA's website at: [HYPERLINK "http://www.epa.gov/ccr" \h]. Information about private wells can be found here: [HYPERLINK "http://www.epa.gov/privatewells" \h].

Also, if your public water system participated in collecting monitoring data for UCMR 1, you can find information about your system at: [HYPERLINK "https://www.epa.gov/dwucmr/first-unregulated-contaminant-monitoring-rule"].

I live in a community with elevated perchlorate levels. Who do I call to get more information about what my utility is doing to address the elevated levels?
Contact your local water supplier to find out more about perchlorate in your drinking water. If you don't know who your local water supplier is, the information should be included in your latest water bill.

I get my tap water from a private well. How can I find out if perchlorate are in my water?
If you are concerned about the possibility of perchlorate in your drinking water and you are served by a private well, EPA recommends testing your drinking water. Approved laboratories can analyze a sample of your water to determine whether perchlorates are present and at what concentrations. Your local water or health department or drinking water system should know if there is such a program in your area. In addition, EPA recommends that residents reach out to their local public health department or state who may be able to help provide support for testing or to seek such support from a responsible party. If no program has been established or support is not available in your area, you can pay to have independent testing done at a qualified testing lab (typical cost is several hundred dollars per sample).

More information about private wells can be found here: [HYPERLINK "http://www.epa.gov/privatewells" \h].

Can a person drink tap water containing perchlorate at or below the level of the health advisory every day of their life and not expect adverse health effects from these chemicals?
Yes, the EPA health advisory level offers a margin of protection for all Americans from adverse health effects for a lifetime of exposure to perchlorate in drinking water at 15ppb.

Can perchlorate be boiled out of my water?
No, perchlorate cannot be removed by heating or boiling water.

Should I be worried about reconstituting my child's infant formula with tap water?
Refer to FDA

Should I consider taking iodine dietary supplements if I am worried about perchlorate?
Refer to FDA

How does a utility reduce/remove perchlorate?
A number of options are available to drinking water systems to lower concentrations of perchlorate in the drinking water supply. In some cases, drinking water systems may be able to reduce concentrations of perchlorate by closing contaminated wells or changing rates of blending of water sources. Perchlorate can be removed using a number of advanced treatment techniques. Each technique has advantages and disadvantages depending on the level of perchlorate present in the source water, removal goals, other water quality parameters, competing treatment objectives, and treatment waste

disposal options. Regenerable and single-pass ion exchange, reverse osmosis, and fixed- and fluidized-bed biological treatment can all remove perchlorate from drinking water sources.

These treatment systems are used by some public water systems today, but should be carefully designed and maintained to ensure that they are effective for treating perchlorate.

Home drinking water treatment units are typically certified by independent third party organizations against ANSI (American National Standards Institute) standards to verify their contaminant removal claims. Some home filters remove impurities using reverse osmosis; however, there currently are no ANSI protocols for testing home treatment systems to verify that these devices effectively remove perchlorate or how frequently the filters should be changed in order to maintain removal efficiency.

Can I buy a home treatment device to remove perchlorate?
If you are concerned about perchlorate in your drinking water, you may consider purchasing a home treatment device such as a filter. However, in order to make a well-informed and cost-effective decision, consider checking with your water system or consumer confidence report to learn about the amount of total perchlorate in your water and identifying a device that has been independently certified to remove perchlorate.

[HYPERLINK "http://www.nsf.org/consumer-resources/what-is-nsf-certification/water-filters-treatment-certification/contaminant-reduction-claims-guide" \t "_blank"], the [HYPERLINK "https://www.wqa.org/" \t "_blank"], [HYPERLINK "http://ul.com/" \t "_blank"] and [HYPERLINK "http://www.csagroup.org/global/en/services/testing-and-certification" \t "_blank"] all certify home treatment products for removal of contaminants. The relevant perchlorate removal standard is [HYPERLINK "http://www.nsf.org/consumer-resources/health-and-safety-tips/water-quality-treatment-tips/standards-for-water-treatment-systems" \t "_blank"]. If you choose to use a home treatment device, it is very important to follow the manufacturer's operation and maintenance instructions carefully in order to make sure the device works properly.

Does perchlorate have a health advisory level?
Yes, on January 8, 2009, EPA released an interim drinking water health advisory of 15 parts of perchlorate for every billion parts of water (parts per billion or ppb). For more information on the Interim Drinking Water Health Advisory for perchlorate can be found here: [HYPERLINK "http://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P1004X7Q.txt"]

Has a safe level of exposure for perchlorate been established?
On February 11, 2011, EPA determined that perchlorate meets the Safe Drinking Water Act criteria for regulation as a contaminant. The Agency found that perchlorate may have an adverse effect on the health of persons and is known to occur in public drinking water systems with a frequency and at levels that present a public health concern. Since that time, EPA has been reviewing the best available scientific data on a range of issues related to perchlorate in drinking water including its occurrence, treatment technologies, analytical methods and the costs and benefits of potential standards.

There also have been state actions on perchlorate standards, guidelines, and advisories. In 2006, Massachusetts adopted a drinking water standard for perchlorate of 2 µg/L, and in 2007, California promulgated a standard of 6 µg/L. Twelve other states have established non-enforceable guidance

levels, action or advisory levels. Depending on the state, a particular level may require a public water system to notify the public, serve as a screening tool for further action, or guide clean-up actions.

Customers that are served by a public water system can contact their local water supplier and ask for information on perchlorate in their drinking water, and are encouraged to request a copy of their Consumer Confidence Report. This report lists the levels of contaminants that have been detected in the water, including those by EPA, and whether the system meets state and EPA drinking water standards.

PEER REVIEW QUESTIONS

Why is EPA conducting a peer review?
EPA will ask peer reviewers to comment on products that the agency will use to inform decision making on perchlorate under the Safe Drinking Water Act

EPA believes that peer review is an important component of the scientific process. The critical feedback, suggestions, and new ideas provided by the peer reviewers stimulate creative thought, strengthen the interpretation of the reviewed material, and confer credibility on the product. The peer review objective is to provide advice to EPA on steps that will yield a highly credible scientific product that is supported by the scientific community.

What products will be reviewed?
Peer reviewers will be asked to comment on the draft report entitled "Peer Review Draft: Proposed Approach to Inform the Derivation of a Maximum Contaminant Level Goal for Perchlorate in Drinking Water." Additionally, EPA is seeking public comments on the peer review charge and the interim list of expert peer review panel candidates.

Where can I find the review products?
All documents in the docket are listed on the [HYPERLINK "http://www.regulations.gov"] website under Docket ID Numbers EPA-HQ-OW-2016-0438 and EPA-HQ-OW-2016-0439.

Can I provide comments on the review products?
Yes. The public will have an opportunity to review and comment on the draft charge questions, the interim list of peer reviewers and the draft report describing application of the model to inform decision making on perchlorate in drinking water.

Additionally, we intend to allow for people to make brief statements during the meeting, and any Safe Drinking Water Act decisions on perchlorate will be subject to public notice and comment.

How long is the comment period?
EPA announced that it's seeking public comments on two separate sets of materials. The first set is the interim list of peer review candidates and the draft charge questions. People should send their comments to Versar, Inc. no later than 21 days after publication in the Federal Register.

A companion notice, also published on the same date, requests comments on the draft scientific report on application of the model to inform decision making on perchlorate. People should send their comments to the docket no later than 45 days after publication in the Federal Register.

Perchlorate Peer Review
Communications Plan

Will the review panelists see my comments or just EPA?
EPA will provide panelists a summary of the public comments submitted on the draft products.

When and where will EPA hold the meeting?
The meeting is projected to occur during in the late fall of 2017 (exact date to be determined). EPA will announce the meeting in the Federal Register at least 30 days in advance to provide the meeting date, location and registration information. EPA anticipates holding the two-day meeting in the Washington, DC metro area.

What will EPA do with the public comments and panel recommendations?
A peer review summary report will be developed that contains the full final comments and recommendations from the peer reviewers. EPA will make the final peer review report available to the public.

EPA will consider any public comments and peer reviewer comments submitted in accordance with the Federal Register notice when finalizing the documents.

How will the contractor select the reviewers?
The contractor considered and screened all candidates against the selection criteria described in the March 1, 2016, and June 3, 2016, Federal Register notices (81 FR 10617 and 81 FR 35760, respectively) which included being free of any conflict of interest and being available to participate in-person in the peer review meeting.

Following the screening process, the list was narrowed to 12 candidates. EPA is now soliciting comments on the interim list of 12 candidates. Once the public comments on the interim list of candidates have been reviewed and considered, and the Science Integrity Official has been consulted, the final list of peer reviewers will be selected.

What happens next?
Once the public comments on the interim list of candidates have been reviewed and considered, the final list of peer reviewers will be selected.

What happens after the peer reviewers are selected?
Following the selection process, the peer reviewers will be tasked with evaluating and providing written comments on the draft products. Additionally, peer reviewers will be provided a summary of public comments and will be provided with the full set of public comments submitted during the draft document's public comment period.

When will EPA establish a national drinking water standard for perchlorate?
EPA will to consider public comments and peer reviewer comments submitted in accordance with the Federal Register notice when finalizing the peer review products. After the peer review is complete, EPA will take the next appropriate steps.

Why is it taking so long for EPA to regulate perchlorate?
In 2011, EPA announced its decision to regulate perchlorate under the Safe Drinking Water Act (SDWA).

Perchlorate Peer Review
Communications Plan

In accordance with SDWA, the Agency requested EPA's Science Advisory Board (SAB) to review how to consider available data in deriving a Maximum Contaminant Level Goal (MCLG) for use in developing a perchlorate National Primary Drinking Water Regulation. The SAB released its final report on May 29, 2013 and recommended that EPA use a novel scientific modeling approach.

The agency, with contributions from Food and Drug Administration scientists, spent over three years to develop the model that predicts changes in thyroid hormone levels that result from exposure to perchlorate. We also assessed epidemiology studies that link thyroid hormone changes to developmental effects. EPA convened a peer review panel to provide recommendations on the model in January 2017 and revised the model considering the comments received in the peer review report submitted to the agency on March 29, 2017. EPA is now initiating the second stage of peer review on scientific materials to support decision making on perchlorate.

INTERNAL QUESTIONS AND ANSWERS

What is the status of the NRDC complaint
On February 18, 2016, the Natural Resource Defense Council filed a complaint in the United States District Court for the Southern District of N.Y. alleging that EPA failed to perform a nondiscretionary duty under SDWA to propose and finalize a national primary drinking water regulation for perchlorate. On October 18, 2016, the court approved a consent decree establishing dates for –

- completing the peer review process (10/18/17, non-enforceable);
- if peer review not complete by 10/18/2017, filing a peer review status report (10/30/17); and
- signature of a proposed and final rule (10/31/18 and 12/19/19, respectively).

Will the peer review products present alternative MCLGs?
No, the documents will not present alternative MCLGs. The documents present various scientific approaches for understanding the potential health impacts from exposure to perchlorate in drinking water. However some experts can be expected to use the scientific methodologies described in the report to speculate how the Agency may derive an MCLG.

Will the methodologies that will be presented to the peer reviewers result in MCLGs that are in the range of MCLs set by California (6 µg/L) and Massachusetts (2 µg/L)?
We do not yet know. The draft analysis could result in values higher than currently used. However, the upcoming peer review of the scientific assessment is an important factor in our understanding of the science.

What is our evaluation of perchlorate occurrence data?

The UCMR 1 perchlorate dataset is the best available nationally representative data on perchlorate occurrence in public water systems. Analytical detections of perchlorate at or above the minimum reporting level (4 µg/L) were identified in about 4% (155 of 3,865) of these systems. EPA estimates that between 5.1 million to 16.6 million people served by the sampled systems could be exposed to perchlorate in drinking water. While perchlorate analytical detections are fairly numerous and widespread geographically, the UCMR 1 findings indicate that perchlorate occurs at relatively low levels: about 85% of analytical perchlorate detections are less than 13 µg/L and 42% are less than 6 µg/L.

However, commenters have pointed out limitations of UCMR 1 for estimating current occurrence. The minimum reporting level is 4 µg/L. Since UCMR 1 data has been collected 2 states have enacted perchlorate standards (CA & MA) and remediation activities or new sources of perchlorate may have impacted concentration levels in public water systems.

Are there any cross-office implications of promulgating a drinking water regulation?
Yes, a drinking water regulation for perchlorate would become the applicable or relevant and appropriate requirement (ARAR) and would replace the current preliminary remediation goal (PRG) for CERCLA sites (current PRG is based on the Interim Drinking Water Health Advisory level of 15 µg/L).

Is there an Environmental Justice/Equity component for the affected communities?
Each community faces unique challenges when addressing concerns related to environmental issues. Perchlorates in drinking water are related to localized sources of contamination often near where these produced have been manufactured or produced. Currently, if water sampling results confirm that drinking water contains perchlorate at individual or combined concentrations greater than 15 parts per billion, water systems should undertake additional sampling to assess the level, scope and localized source of contamination to inform next steps.

How will the RfD, or the interim health advisory, be used to inform the MCLG?
Based on SAB recommendations EPA does not intend to use the perchlorate RfD to inform derivation of an MCLG. The SAB stated that it, ". . . recognizes that this is a novel approach as compared to previous MCLG derivations that use the RfD and exposure factors. However, PBPK/PDIUI modeling provides a more rigorous tool to integrate the totality of information available on perchlorate, and this approach may better address different life stage susceptibilities to perchlorate than the default MCLG approach."

Message

From: Tricas, Marisa [tricas.marisa@epa.gov]
Sent: 9/6/2017 4:27:41 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: One More Question: Perchlorate Roll-out plan.
Attachments: Perchlorate Peer Review Roll Out_09.06.17.Final.docx

Edits incorporated, with new comments from Jennifer merged.

Sincerely,

Marisa Tricas
Communications Specialist
Office of Ground Water and Drinking Water
United States Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington, D.C. 20004
Office: 202-564-2955
Mobile: 202-770-5092
Office: WJC East 2104D
Website: https://www.epa.gov/ground-water-and-drinking-water

From: Christ, Lisa
Sent: Wednesday, September 6, 2017 12:23 PM
To: Tricas, Marisa <tricas.marisa@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Subject: RE: One More Question: Perchlorate Roll-out plan.

Thanks for talking through the questions with me ☺

From: Tricas, Marisa
Sent: Wednesday, September 06, 2017 12:14 PM
To: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: One More Question: Perchlorate Roll-out plan.

No worries. Thanks Crystal, also apologies for the quick turn-around on this. OW changed the deadline to noon today.

Marisa

From: Rodgers-Jenkins, Crystal
Sent: Wednesday, September 6, 2017 12:10 PM
To: Tricas, Marisa <tricas.marisa@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: One More Question: Perchlorate Roll-out plan.

Marisa,

I am just seeing this. I have to defer to Lisa.

-Crystal

From: Tricas, Marisa
Sent: Wednesday, September 06, 2017 11:32 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Subject: One More Question: Perchlorate Roll-out plan.
Importance: High

Hi Lisa and Crystal,

Jennifer got back to me with the Perchlorate Roll-out plan comments. One question remaining she had is if you can add all the stakeholders and federal partners that participated in the meetings thus far to the list. OW Comms needs this by noon.

Also if Mike approves the 09/11 date, we will need to notify our stakeholders tomorrow. I will coordinate up with here with Peter and Jennifer but will likely copy you both on these as I do not want to duplicate efforts.

Thanks so much.

Sincerely,

Marisa Tricas
Communications Specialist
Office of Ground Water and Drinking Water
United States Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington, D.C. 20004
Office: 202-564-2955
Mobile: 202-770-5092
Office: WJC East 2104D
Website: https://www.epa.gov/ground-water-and-drinking-water

Message

From: Tricas, Marisa [tricas.marisa@epa.gov]
Sent: 9/6/2017 3:32:20 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]; Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]
Subject: One More Question: Perchlorate Roll-out plan.
Attachments: MCLG.Perchlorate Roll Out_09.05.17.Finaldocx.jlm.docx

Importance: High

Hi Lisa and Crystal,

Jennifer got back to me with the Perchlorate Roll-out plan comments. One question remaining she had is if you can add all the stakeholders and federal partners that participated in the meetings thus far to the list. OW Comms needs this by noon.

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Marisa Tricas
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United States Environmental Protection Agency
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Washington, D.C. 20004
Office: 202-564-2955
Mobile: 202-770-5092
Office: WJC East 2104D
Website: https://www.epa.gov/ground-water-and-drinking-water

Message

From: El Burai Felix, Alia [ElBuraiFelix.Alia@epa.gov]
Sent: 9/6/2017 12:16:33 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: ADVANCE NOTIFICATION -- ORD-023135 Wang et al. Screening of ToxCast Phase I Chemicals in the NIS Assay (Iodide transport)
Attachments: NIS_phase_one manuscript v12 8.29.17.docx; Supplemental Fig 1 and Table 1.docx; Supplemental Fig 2. Dose-Response Curves.pdf; Supplemental Fig 3. Control Curves.pdf; Supplemental File 1. Documented Data Analysis in R.HTML; Supplemental_Table_2.csv; WangFactSheet8.23.17.docx

Hi, Lisa!

Hope you are well. Nicole sent me this email today asking me if I knew someone from TAB, specifically from the perchlorate team, that might be interested in doing a policy review. I asked Ahmed if he was interested. Do you have someone else in mind? Thanks in advance!

Best regards,

Alia El Burai Félix, MS
Physical Scientist
U.S. Environmental Protection Agency (US EPA)
Office of Groundwater and Drinking Water (OGWDW)
Standards and Risk Management Division (SRMD)
Targeting and Analysis Branch (TAB)

Address: EPA East Bldg. Rm. 2357G
Office: 202-566-2572
Email: ElBuraiFelix.Alia@epa.gov

From: Tucker, Nicole
Sent: Wednesday, September 6, 2017 7:46 AM
To: El Burai Felix, Alia <ElBuraiFelix.Alia@epa.gov>
Subject: FW: ADVANCE NOTIFICATION -- ORD-023135 Wang et al. Screening of ToxCast Phase I Chemicals in the NIS Assay (Iodide transport)

Hi Alia,
Hope you are doing well. Ryan Albert has asked me to coordinate with appropriate TAB person for this manuscript, to ask them to review. The manuscript is about endocrine disruptors that disrupt the thyroid.
In the fact sheet for the manuscript it mentions "Monovalent anions, such as the environmental contaminant perchlorate, have been well characterized as competitive inhibitors of NIS-mediated uptake of iodide, but limited information exists for more structurally diverse chemicals."
I am thinking someone from the perchlorate team would be best suited to review. ORD is looking for a policy review, but if someone has other comments that could provide those as well if they wanted.
Do you have a person in mind that would be best suited to review this manuscript that I could ask? Thanks Alia.
-Nicole

Nicole Tucker
US Environmental Protection Agency
Office of Ground Water and Drinking Water
Standards and Risk Management Division
202-564-1946

From: Albert, Ryan
Sent: Tuesday, September 05, 2017 4:23 PM
To: Tucker, Nicole <Tucker.Nicole@epa.gov>
Cc: Holsinger, Hannah <Holsinger.Hannah@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Hautman, Dan <Hautman.Dan@epa.gov>; Carroll, Gregory <Carroll.Gregory@epa.gov>
Subject: FW: ADVANCE NOTIFICATION -- ORD-023135 Wang et al. Screening of ToxCast Phase I Chemicals in the NIS Assay (Iodide transport)

Hi Nicole,

Working with Hannah and coordinating with the designated TAB lead, please review the attached document and prepare comments for our review by COB Thursday, September 14. We will shoot to get comments back to OST no later than the 18th.

Thank you!
Ryan

Ryan Albert, Ph.D.
Acting Chief
Standards and Risk Reduction Branch
Office of Ground Water and Drinking Water
United States Environmental Protection Agency
(202) 564-0763

From: Rodgers-Jenkins, Crystal
Sent: Tuesday, September 05, 2017 3:49 PM
To: Albert, Ryan <Albert.Ryan@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Hautman, Dan <Hautman.Dan@epa.gov>; Carroll, Gregory <Carroll.Gregory@epa.gov>
Subject: FW: ADVANCE NOTIFICATION -- ORD-023135 Wang et al. Screening of ToxCast Phase I Chemicals in the NIS Assay (Iodide transport)

I think this paper mostly related to SRRB's oversight of the agency's Endocrine Disruptor Screening Program. However, TAB should be aware of this high throughput screening in the context of future CCLs.

SRRB, please take the lead in reviewing the paper. For others, if your unit plans to also review, please let SRRB know so they can expect to receive your comments before the deadline. Thanks.

Abstract. The U.S. EPA's Endocrine Disruptor Screening Program (EDSP) and Office of Research and Development (ORD) are currently developing high throughput assays to screen chemicals that may alter the thyroid hormone pathway. One potential target in this pathway is the sodium iodide symporter (NIS), a transmembrane glycoprotein that mediates iodide uptake into the thyroid gland as the initial step in thyroid hormone biosynthesis. Our laboratory recently validated a screening approach to identify potential NIS inhibitors using a novel cell line hNIS-HEK293T-EPA. Here, we screened the ToxCast phase 1_v2 chemical library, representing 293 unique environmental chemicals, in the newly developed radioactive iodide uptake (RAIU) assay. First, 310 blinded samples were screened in single-concentration format at 100μM. Using 20% inhibition as the activity threshold, 169 samples reached this criterion and were further tested for concentration-response (0.001 μM - 100 μM) with parallel RAIU and cell viability assays. To facilitate prioritization of potential thyroid toxicants, a unique ranking system that incorporates cytotoxicity responses was developed to sort the RAIU inhibition potency of the chemicals. Chemicals were ranked with a score that is relative to

the well-known NIS inhibitor sodium perchlorate. The top ranked 14 chemicals had varying responses in the screening and their diverse toxicological properties are discussed in detail. Further testing is warranted to characterize the nature of the inhibition observed with these chemicals. This study represents the first large-scale screening of environmental chemicals for NIS inhibitors, and supports the U.S. EPA's EDSP21 and OECD in their efforts to develop high throughput screening approaches that expand the coverage of molecular targets of thyroid disruption.

From: Behl, Betsy
Sent: Tuesday, September 05, 2017 3:29 PM
To: Strong, Jamie <Strong.Jamie@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Cc: Emerson, Vanessa <emerson.vanessa@epa.gov>
Subject: FW: ADVANCE NOTIFICATION -- ORD-023135 Wang et al. Screening of ToxCast Phase I Chemicals in the NIS Assay (Iodide transport)

Jamie, please let me know if you can meet the deadline for comments requested by ORD. looks like an interesting paper. Crystal let us know if your folks want to provide comments or not. Happy to include them.

Betsy

From: Tietge, Joe
Sent: Tuesday, September 05, 2017 11:57 AM
To: Keigwin, Richard <Keigwin.Richard@epa.gov>; Vogel, Dana <Vogel.Dana@epa.gov>; Barone, Stan <Barone.Stan@epa.gov>; Behl, Betsy <Behl.Betsy@epa.gov>; Bahadori, Tina <Bahadori.Tina@epa.gov>; Ohanian, Edward <Ohanian.Edward@epa.gov>
Cc: Frithsen, Jeff <Frithsen.Jeff@epa.gov>; Rodan, Bruce <rodan.bruce@epa.gov>; Benson, William <Benson.William@epa.gov>; Hines, Ronald <Hines.Ronald@epa.gov>; Sjogren, Mya <Sjogren.Mya@epa.gov>; Osaka, Anna <Osaka.Anna@epa.gov>; D'Amico, Louis <DAmico.Louis@epa.gov>
Subject: ADVANCE NOTIFICATION -- ORD-023135 Wang et al. Screening of ToxCast Phase I Chemicals in the NIS Assay (Iodide transport)

Good morning:
ORD is providing advanced notification of a recently developed manuscript entitled: ***High-Throughput Screening of ToxCast Phase I Chemical Library for Sodium Iodide Symporter (NIS) Inhibitors*** by Wang, et al. This paper presents a novel *in vitro* screening approach that was developed to rapidly identify chemicals that can inhibit the uptake of iodide by the thyroid and disrupt the synthesis of thyroid hormones. The assay targets a key molecular initiating event, the uptake of iodide as mediated by the thyroid sodium iodide symporter (NIS), within the thyroid hormone pathway. This assay was used to screen the ToxCast Phase 1 chemical library.

The screening and ranking of 293 chemicals in this study represents the first large scale effort to investigate NIS as a molecular target of environmental chemicals that covers a broad spectrum of structural and toxicological properties. This assay and ranking approach can now be used for screening other, larger chemical libraries such as the ToxCast Phase 2 and E1K libraries.

The goal of this advanced notification is to provide our colleagues a heads-up concerning important ORD products so as avoid any surprises and to provide you the opportunity to review products for policy relevant concerns. **We ask for your comments by COB September 19.**

Please provide any comments you might have to Jeff Frithsen. Meanwhile, if you have questions, please contact me.
Thank you!
Joe

Joseph E. Tietge
Assistant Laboratory Director

National Health and Environmental Effects Research Laboratory
US EPA
6201 Congdon Blvd.
Duluth, MN 55804

T 218-529-5176
F 218-529-5003
C 218-355-1702

High-Throughput Screening of ToxCast Phase I Chemical Library for Sodium Iodide Symporter (NIS) Inhibitors

Jun Wang[*,†], Daniel R. Hallinger[†], Ashley S. Murr[†], Angela R. Buckalew[†], Steven O. Simmons[‡], Susan C. Laws[†,1], Tammy E. Stoker[†,1]

[*]Oak Ridge Institute for Science and Education, US Department of Energy, Oak Ridge, TN 37831, USA;

[†]Endocrine Toxicology Branch, Toxicity Assessment Division, National Health and Environmental Effects Research Laboratory, Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, NC, 27711, USA.

[‡]National Center for Computational Toxicology, Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, NC, 27711, USA

[1] Corresponding authors: Contact at Endocrine Toxicology Branch, Toxicity Assessment Division (MD B105-04), National Health and Environmental Effects Research Laboratory, U.S. Environmental Protection Agency, 109 T.W. Alexander Drive, Research Triangle Park, NC, 27711. E-mail/Phone: laws.susan@epa.gov (1 919 541-0173) and stoker.tammy@epa.gov (1 919 541-2783)

DISCLAIMER: This manuscript has been reviewed in accordance with the policies of the National Health and Environmental Effects Research Laboratory and National Center for Computational Toxicology, Office of Research and Development, U.S. Environmental Protection Agency, and approved for publication. Approval does not signify that the contents necessarily reflect the views or policy of the Agency nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

Abstract

The U.S. EPA's Endocrine Disruptor Screening Program (EDSP) and Office of Research and Development (ORD) are currently developing high throughput assays to screen chemicals that may alter the thyroid hormone pathway. One potential target in this pathway is the sodium iodide symporter (NIS), a transmembrane glycoprotein that mediates iodide uptake into the thyroid gland as the initial step in thyroid hormone biosynthesis. Our laboratory recently validated a screening approach to identify potential NIS inhibitors using a novel cell line hNIS-HEK293T-EPA. Here, we screened the ToxCast phase 1_v2 chemical library, representing 293 unique environmental chemicals, in the newly developed radioactive iodide uptake (RAIU) assay. First, 310 blinded samples were screened in single-concentration format at 100μM. Using 20% inhibition as the activity threshold, 169 samples reached this criterion and were further tested for concentration-response (0.001 μM - 100 μM) with parallel RAIU and cell viability assays. To facilitate prioritization of potential thyroid toxicants, a unique ranking system that incorporates cytotoxicity responses was developed to sort the RAIU inhibition potency of the chemicals. Chemicals were ranked with a score that is relative to the well-known NIS inhibitor sodium perchlorate. The top ranked 14 chemicals had varying responses in the screening and their diverse toxicological properties are discussed in detail. Further testing is warranted to characterize the nature of the inhibition observed with these chemicals. This study represents the first large-scale screening of environmental chemicals for NIS inhibitors, and supports the U.S. EPA's EDSP21 and OECD in their efforts to develop high throughput screening approaches that expand the coverage of molecular targets of thyroid disruption.

Keywords: sodium iodide symporter, thyroid, endocrine disruptor, high-throughput *in vitro* screening assay

Introduction

Thyroid hormones (TH; i.e., thyroxine (T4) and triiodothyronine (T3)) regulate an array of physiological processes that are essential for metabolism, cardiovascular function, bone maintenance, as well as fetal and post-natal neurodevelopment [ADDIN EN.CITE ADDIN EN.CITE.DATA]. Over the past two decades, a number of structurally diverse xenobiotics have been shown to interfere with TH homeostasis and result in physiological and morphological perturbations [ADDIN EN.CITE ADDIN EN.CITE.DATA]. Further work in this area has identified multiple molecular targets of chemical-mediated thyroid disruption including the regulation of circulating TH through feedback mechanisms within the hypothalamic-pituitary-thyroid (HPT) axis, TH synthesis and secretion, TH distribution and transport, TH metabolism, and TH receptor binding and action [ADDIN EN.CITE ADDIN EN.CITE.DATA]. These studies demonstrated a need for a better understanding of the structural characteristics of chemicals with thyroid disrupting activity, the potential for environmental exposures, and the possible health risks to humans and wildlife. To address these concerns, the U.S. EPA's Endocrine Disruptor Screening Program (EDSP21, https://www.epa.gov/endocrine-disruption) in concert with the U.S. EPA's Office of Research and Development (ORD) recently expanded the coverage of molecular targets for disruption of the TH pathway by developing and implementing the use of high throughput screening (HTS) assays to identify inhibitors of TH synthesis (e.g., sodium/iodide symporter (NIS) and thyroid peroxidase) and T4 metabolism (e.g., deiodinases). Methods for a thyroid peroxidase assay were previously described by Paul et al. (2014) and used to screen chemicals in the ToxCast phase I_v2 and II chemical libraries [ADDIN EN.CITE

<EndNote><Cite><Author>Paul Friedman</Author><Year>2016</Year><RecNum>82</RecNum><DisplayText>(Paul Friedman<style face="italic"> et al.</style>, 2016)</DisplayText><record><rec-number>82</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1493395974">82</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Paul Friedman, Katie</author><author>Watt, Eric D.</author><author>Hornung, Michael W.</author><author>Hedge, Joan M.</author><author>Judson, Richard S.</author><author>Crofton, Kevin M.</author><author>Houck, Keith A.</author><author>Simmons, Steven O.</author></authors></contributors><titles><title>Tiered High-Throughput Screening Approach to Identify Thyroperoxidase Inhibitors Within the ToxCast Phase I and II Chemical Libraries</title><secondary-title>Toxicological Sciences</secondary-title></titles><periodical><full-title>Toxicological Sciences</full-title></periodical><pages>160-180</pages><volume>151</volume><number>1</number><dates><year>2016</year></dates><isbn>1096-6080</isbn><urls><related-urls><url>http://dx.doi.org/10.1093/toxsci/kfw034</url></related-urls></urls><electronic-resource-num>10.1093/toxsci/kfw034</electronic-resource-num></record></Cite></EndNote>]. In addition, our laboratory recently demonstrated the utility of another HTS assay to detect chemicals that disrupt NIS-mediated transport of extracellular iodide across the cellular membrane [ADDIN EN.CITE

<EndNote><Cite><Author>Hallinger</Author><Year>2017</Year><RecNum>64</RecNum><DisplayText>(Hallinger<style face="italic"> et al.</style>, 2017)</DisplayText><record><rec-number>64</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1490798592">64</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Hallinger, Daniel R.</author><author>Murr, Ashley S.</author><author>Buckalew, Angela R.</author><author>Simmons, Steven O.</author><author>Stoker, Tammy E.</author><author>Laws, Susan C.</author></authors></contributors><titles><title>Development of a screening approach to detect thyroid disrupting chemicals that inhibit the human sodium iodide symporter (NIS)</title><secondary-title>Toxicology in Vitro</secondary-title></titles><periodical><full-title>Toxicology in Vitro</full-title></periodical><pages>66-78</pages><volume>40</volume><keywords><keyword>Thyroid</keyword><keyword>Endocrine disruptors</keyword><keyword>Sodium iodide symporter</keyword><keyword>Chemical screening</keyword></keywords><dates><year>2017</year><pub-dates><date>4//</date></pub-dates></dates><isbn>0887-2333</isbn><urls><related-urls><url>http://www.sciencedirect.com/science/article/pii/S0887233316302569</url><url>http://ac.els-cdn.com/S0887233316302569/1-s2.0-S0887233316302569-main.pdf?_tid=286edb04-d8fa-11e6-b2db-00000aacb360&acdnat=1484248141_9bcc422b76262b7c7843748a566dbb7c</url></relate

d-urls></urls><electronic-resource-num>http://dx.doi.org/10.1016/j.tiv.2016.12.006</electronic-resource-num></record></Cite></EndNote>].

NIS is a glycoprotein with 13 transmembrane helices [ADDIN EN.CITE ADDIN EN.CITE.DATA] that actively transports I^- anions into thyroid follicular cells. This activity relies on the inwardly directed Na^+ electrochemical gradient maintained by Na^+/K^+ ATPases with an electrogenic stoichiometry of 2 Na^+ per I^- [ADDIN EN.CITE ADDIN EN.CITE.DATA]. Under normal physiological conditions, NIS can efficiently enrich iodide into the thyroid gland to achieve a 20 to 40 fold I^- concentration gradient [ADDIN EN.CITE <EndNote><Cite><Author>Dohán</Author><Year>2003</Year><RecNum>5</RecNum><DisplayText>(Dohán<style face="italic"> et al.</style>, 2003)</DisplayText><record><rec-number>5</rec-number><foreign-keys><key app="EN" db-id="09vdaavf8zzsfkefza7x90s6tasptssaefxe" timestamp="1493133346">5</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Dohán, Orsolya</author><author>De la Vieja, Antonio</author><author>Paroder, Viktoriya</author><author>Riedel, Claudia</author><author>Artani, Mona</author><author>Reed, Mia</author><author>Ginter, Christopher S.</author><author>Carrasco, Nancy</author></authors></contributors><titles><title>The Sodium/Iodide Symporter (NIS): Characterization, Regulation, and Medical Significance</title><secondary-title>Endocrine Reviews</secondary-title></titles><periodical><full-title>Endocrine Reviews</full-title></periodical><pages>48-77</pages><volume>24</volume><number>1</number><dates><year>2003</year></dates><i

sbn>0163-769X</isbn><urls><related-urls><url>http://dx.doi.org/10.1210/er.2001-0029</url></related-urls></urls><electronic-resource-num>10.1210/er.2001-0029</electronic-resource-num></record></Cite></EndNote>]. Apart from the thyroid gland, NIS is also expressed in other tissues such as mammary gland during lactation, stomach, and salivary gland [ADDIN EN.CITE ADDIN EN.CITE.DATA]. Disruption of NIS-mediated iodide uptake has been correlated with depressed TH synthesis (hypothyroidism) and adverse health outcomes in humans and animals. For example, patients with various gene mutations leading to aberrant NIS protein have hypothyroidism [ADDIN EN.CITE <EndNote><Cite><Author>Pohlenz</Author><Year>1999</Year><RecNum>97</RecNum><DisplayText>(Pohlenz and Refetoff, 1999)</DisplayText><record><rec-number>97</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1494530226">97</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Pohlenz, Joachim</author><author>Refetoff, Samuel</author></authors></contributors><titles><title>Mutations in the sodium/iodide symporter (NIS) gene as a cause for iodide transport defects and congenital hypothyroidism</title><secondary-title>Biochimie</secondary-title></titles><periodical><full-title>Biochimie</full-title></periodical><pages>469-476</pages><volume>81</volume><number>5</number><keywords><keyword>congenital hypothyroidism</keyword><keyword>thyroid</keyword><keyword>iodide transport</keyword><keyword>molecular genetics</keyword></keywords><dates><year>1999</year><pub-dates><date>5//</date></pub-dates></dates><isbn>0300-9084</isbn><urls><related-

urls><url>http://www.sciencedirect.com/science/article/pii/S0300908499800972</url></related-urls></urls><electronic-resource-num>https://doi.org/10.1016/S0300-9084(99)80097-2</electronic-resource-num></record></Cite></EndNote>]. In addition, several monovalent anions including perchlorate (ClO_4^-), thiocyanate (SCN^-), and nitrate (NO_3^-) are known to competitively inhibit I^- uptake by NIS and disrupt TH synthesis in humans [ADDIN EN.CITE ADDIN EN.CITE.DATA] and multiple species of vertebrates [ADDIN EN.CITE ADDIN EN.CITE.DATA]. The identification of the environmental chemicals triclosan, triclocarban, BDE-47, bisphenol A (Wu *et al.*, 2016), and several small drug-like organic molecules as NIS-mediated iodide transport inhibitors [ADDIN EN.CITE ADDIN EN.CITE.DATA] indicates effects on NIS that extend beyond simple competitive inhibition by anions.

We recently developed a radioactive iodide uptake (RAIU) assay to measure uptake of iodide in a novel cell line stably expressing human sodium/iodide symporter, hNIS-HEK293T-EPA [ADDIN EN.CITE

<EndNote><Cite><Author>Hallinger</Author><Year>2017</Year><RecNum>64</RecNum><DisplayText>(Hallinger<style face="italic"> et al.</style>, 2017)</DisplayText><record><rec-number>64</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1490798592">64</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Hallinger, Daniel R.</author><author>Murr, Ashley S.</author><author>Buckalew, Angela R.</author><author>Simmons, Steven O.</author><author>Stoker, Tammy E.</author><author>Laws, Susan

C.</author></authors></contributors><titles><title>Development of a screening approach to detect thyroid disrupting chemicals that inhibit the human sodium iodide symporter (NIS)</title><secondary-title>Toxicology in Vitro</secondary-title></titles><periodical><full-title>Toxicology in Vitro</full-title></periodical><pages>66-78</pages><volume>40</volume><keywords><keyword>Thyroid</keyword><keyword>Endocrine disruptors</keyword><keyword>Sodium iodide symporter</keyword><keyword>Chemical screening</keyword></keywords><dates><year>2017</year><pub-dates><date>4//</date></pub-dates></dates><isbn>0887-2333</isbn><urls><related-urls><url>http://www.sciencedirect.com/science/article/pii/S0887233316302569</url><url>http://ac.els-cdn.com/S0887233316302569/1-s2.0-S0887233316302569-main.pdf?_tid=286edb04-d8fa-11e6-b2db-00000aacb360&acdnat=1484248141_9bcc422b76262b7c7843748a566dbb7c</url></related-urls></urls><electronic-resource-num>http://dx.doi.org/10.1016/j.tiv.2016.12.006</electronic-resource-num></record></Cite></EndNote>]. This HTS approach was validated and proved to be a robust, highly reproducible approach for rapidly screening large chemical libraries for inhibitors of NIS-mediated iodide uptake. In the current study, we applied the HTS approach to screen the larger ToxCast phase1_v2 chemical library [ADDIN EN.CITE <EndNote><Cite><Author>Richard</Author><Year>2016</Year><RecNum>66</RecNum><DisplayText>(Richard<style face="italic"> et al.</style>, 2016)</DisplayText><record><rec-number>66</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1490798627">66</key></foreign-

keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Richard, Ann M.</author><author>Judson, Richard S.</author><author>Houck, Keith A.</author><author>Grulke, Christopher M.</author><author>Volarath, Patra</author><author>Thillainadarajah, Inthirany</author><author>Yang, Chihae</author><author>Rathman, James</author><author>Martin, Matthew T.</author><author>Wambaugh, John F.</author><author>Knudsen, Thomas B.</author><author>Kancherla, Jayaram</author><author>Mansouri, Kamel</author><author>Patlewicz, Grace</author><author>Williams, Antony J.</author><author>Little, Stephen B.</author><author>Crofton, Kevin M.</author><author>Thomas, Russell S.</author></authors></contributors><titles><title>ToxCast Chemical Landscape: Paving the Road to 21st Century Toxicology</title><secondary-title>Chemical Research in Toxicology</secondary-title></titles><periodical><full-title>Chemical Research in Toxicology</full-title></periodical><pages>1225-1251</pages><volume>29</volume><number>8</number><dates><year>2016</year><pub-dates><date>2016/08/15</date></pub-dates></dates><publisher>American Chemical Society</publisher><isbn>0893-228X</isbn><urls><related-urls><url>http://dx.doi.org/10.1021/acs.chemrestox.6b00135</url></related-urls></urls><electronic-resource-num>10.1021/acs.chemrestox.6b00135</electronic-resource-num></record></Cite></EndNote>]. This library of 293 unique chemicals covers a broad spectrum of chemicals that are currently under the U.S. EPA's regulatory purview [ADDIN EN.CITE

<EndNote><Cite><Author>Richard</Author><Year>2016</Year><RecNum>66</RecNum><DisplayText>(Richard<style face="italic"> et al.</style>, 2016)</DisplayText><record><rec-number>66</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1490798627">66</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Richard, Ann M.</author><author>Judson, Richard S.</author><author>Houck, Keith A.</author><author>Grulke, Christopher M.</author><author>Volarath, Patra</author><author>Thillainadarajah, Inthirany</author><author>Yang, Chihae</author><author>Rathman, James</author><author>Martin, Matthew T.</author><author>Wambaugh, John F.</author><author>Knudsen, Thomas B.</author><author>Kancherla, Jayaram</author><author>Mansouri, Kamel</author><author>Patlewicz, Grace</author><author>Williams, Antony J.</author><author>Little, Stephen B.</author><author>Crofton, Kevin M.</author><author>Thomas, Russell S.</author></authors></contributors><titles><title>ToxCast Chemical Landscape: Paving the Road to 21st Century Toxicology</title><secondary-title>Chemical Research in Toxicology</secondary-title></titles><periodical><full-title>Chemical Research in Toxicology</full-title></periodical><pages>1225-1251</pages><volume>29</volume><number>8</number><dates><year>2016</year><pub-dates><date>2016/08/15</date></pub-dates></dates><publisher>American Chemical Society</publisher><isbn>0893-228X</isbn><urls><related-urls><url>http://dx.doi.org/10.1021/acs.chemrestox.6b00135</url></related-

urls></urls><electronic-resource-num>10.1021/acs.chemrestox.6b00135</electronic-resource-num></record></Cite></EndNote>], as well as a subset of chemicals that have been tested extensively in the Agency's EDSP Tier I Screening Battery [ADDIN EN.CITE <EndNote><Cite><Author>U.S.EPA</Author><Year>2015</Year><RecNum>111</RecNum><DisplayText>(U.S.EPA, 2015)</DisplayText><record><rec-number>111</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1499365200">111</key></foreign-keys><ref-type name="Online Database">45</ref-type><contributors><authors><author>U.S.EPA</author></authors></contributors><titles><title>Endocrine Disruptor Screening Program Tier 1 screening determinations or weight of evidence assessments.</title></titles><dates><year>2015</year><pub-dates><date>July 6, 2017</date></pub-dates></dates><pub-location>https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and</pub-location><urls><related-urls><url>https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-tier-1-screening-determinations-and</url></related-urls></urls></record></Cite></EndNote>]. This study expands the current knowledge of NIS inhibition potential of environmentally-relevant chemicals and the results may be used for prioritizing chemicals for further testing and informing the development of adverse outcome pathways for thyroid disruption.

Materials and Methods

Cell Line and Growth Conditions

As described by Hallinger et al. (2017), an HEK293T cell line expressing functional human NIS, hNIS-HEK293T-EPA, was utilized for radioactive iodide uptake (RAIU) and cell viability assays. In brief, low passage hNIS-HEK293T-EPA cells (<30 passes) were cultured in Dulbecco's Modified Eagle Medium (DMEM; Gibco,Waltham, MA) supplemented with 10% newborn calf serum (Gibco, Waltham, MA), 10mM HEPES, 100U/mL penicillin and 0.1mg/mL streptomycin (Sigma, St. Louis, MO) at 37°C in a humidified 5% CO_2 atmosphere. Culture flasks were coated with collagen type I (Corning, Corning, NY) in 0.02N acetic acid solution (4µg per cm^2) and washed with sterile deionized H_2O prior to subculture. All 96-well microplates were coated with 0.01% poly-L-lysine (Sigma, St. Louis, MO) and washed with sterile deionized H_2O prior to cell seeding. Cells were grown to 90 – 95% confluence in T75 flasks (Corning, Corning, NY) before trypsinization in 0.05% trypsin/EDTA (Gibco, Waltham, MA) where cells were sub-cultured in T75 flasks or seeded in 96-well plates as described in assay sections below.

Chemicals

Chemical names, CAS numbers, and maximum concentration tested are shown in Tables 1 (Assay controls) and 2 (Test chemicals). All control chemicals were initially solubilized in DMSO (EMD Millipore Corp., Darmstadt, Germany) at 20 mM and included sodium perchlorate ($NaClO_4$; RAIU assay positive control), sodium nitrate ($NaNO_3$; RAIU assay EC_{80} control), sodium thiocyanate

(NaSCN; RAIU assay EC_{20} control), 2,4-dichlorophenoxyacetic acid (2,4-D; RAIU assay negative control), and 2,3-dichloro-1,4-napthoquinone (DCNQ; cell viability assay positive) (Sigma Aldrich, St. Louis, MO).

Chemicals of the ToxCast phase 1_v2 library were solubilized in DMSO and provided as 310 blinded samples in five 96-well plates (62 samples per plate) (Evotec Inc., South San Francisco, CA). Of the 310 samples, there were 293 unique chemicals - the remaining 17 serving as internal quality control replicates randomly distributed among the five plates. All chemicals were administered to bioassay plates using a BioMek FX Automated Laboratory Workstation (Beckman Coulter, Indianapolis, IN) equipped with a stainless steel high density replicating (HDR) tool (96-pin) to transport 350nL per well for the RAIU, cell viability, and Sandell-Kolthoff (SK) assays as described below.

Radioactive Iodide Uptake (RAIU) Assay

RAIU assays were conducted as previously described (Hallinger *et al.* 2017). In brief, hNIS-HEK293T-EPA cells were seeded with a MultiFlo FX dispenser (BioTek, Winooski, VT) into ScintiPlate-96 microplates (Perkin Elmer, Waltham, MA) at a density of $4.0x10^4$ cells per well in 200µL growth media and incubated for 40 hours before experimentation. On the day of the assay, carrier-free ^{125}I (Perkin-Elmer, Waltham, MA; specific activity: 17.4Ci/mg) was diluted with Hanks' balanced salt solution (Sigma, St. Louis, MO) supplemented with 10mM HEPES (uptake buffer; pH 7.4) at 5µCi/mL (288pg ^{125}I/mL uptake buffer; 2.30nM). The assay was initiated by gently washing cells twice with 200µL uptake buffer using a 96-well Tecan HydroSpeed plate

washer (Tecan, Männedorf, Switzerland). Uptake buffer (59.7µL) was then added back to each well. Chemical samples (350nL at 200X) were added to each well using the HDR tool as previously described to achieve a 1X chemical/0.5% final DMSO concentration with subsequent addition of 10µL of ^{125}I dilution (final [^{125}I]: 329pM; 2.88pg/well) for a final reaction volume of 70µL/well. With this dilution protocol, a 20 mM stock chemical would have a final test concentration of 100 µM. Cells were incubated at room temperature for 2 hours and then washed twice with 200µL ice-cold uptake buffer. All uptake buffer was aspirated from wells, plates were sealed, and read on a MicroBeta^2 plate reader (Perkin Elmer, Waltham, MA) using a detection protocol to measure CPM corresponding to intracellular ^{125}I concentration. Assays for single and multi-concentration screening of samples were replicated in three independent runs containing different passages of the cells (i.e., 3 independent biological replicates).

Cell Viability Assay

Cell viability assays were conducted in parallel with the RAIU assays to identify samples where a decrease in RAIU might be due to cytotoxicity. hNIS-HEK293T-EPA cells were seeded and grown in 96-well solid white assay plates (Corning, Corning, NY) and exposed to chemical samples as described for RAIU assay. CellTiter-Glo (Promega, Fitchburg, WI) reagent (70µL) was then added to each well and plates were shaken for 5 minutes at 700rpm. Plates were incubated at room temperature for 10 minutes and then read on a FLUOstar Omega plate reader (BMG Labtech, Cary, NC) using an endpoint luminescence protocol (top read) to measure relative light units (RLU) indicative of ATP concentration. Assays for multi-concentration screening of samples were

replicated in three independent runs containing different passages of the cells (i.e., 3 independent biological replicates).

Chemical Screening

Chemicals were tested in a tiered approach to maximize resources and testing efficiency. Initial radioactive iodide uptake (RAIU) assays were performed as a single-concentration screen to identify active samples for subsequent testing in a concentration-response format. Each of the 310 blinded samples was tested at the maximum concentration (100μM, with some exceptions owing to solubility limits, see Table 2) in three independent RAIU assays using distinct passages of hNIS-HEK293T-EPA cells (i.e., bioreplicates). The median response for each sample from the three bioreplicates of the RAIU assays was used to determine whether the sample was active. Chemical samples were identified as active if the median RAIU inhibition was larger than a pre-determined activity threshold (20% in this study, refer to the data analysis section). Putative NIS inhibitors (i.e. active samples) were retested at six concentrations (obtained from 10-fold serial dilutions beginning with the maximum concentration, Table 2) in parallel RAIU and cell viability assays. The assay plate maps for single concentration screening and concentration-response assays are provided in Supplemental Figure 1.

Identification of Iodide Interference using Sandell-Kolthoff Reaction

Sandell-Kolthoff (SK) reaction is a colorimetric method to quantify iodide concentration through measurement of the iodide-catalyzed conversion of Ce^{4+} (yellow) to Ce^{3+} (colorless) [ADDIN EN.CITE ADDIN EN.CITE.DATA]. SK reaction assay was used to detect the presence of

iodide contamination or structural iodide in chemical samples that could possibly interfere with the RAIU assay and cause a false positive response. All 310 samples were tested by SK reaction following a previously developed protocol [ADDIN EN.CITE <EndNote><Cite><Author>Hallinger</Author><Year>2017</Year><RecNum>64</RecNum><DisplayText>(Hallinger<style face="italic"> et al.</style>, 2017)</DisplayText><record><rec-number>64</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1490798592">64</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Hallinger, Daniel R.</author><author>Murr, Ashley S.</author><author>Buckalew, Angela R.</author><author>Simmons, Steven O.</author><author>Stoker, Tammy E.</author><author>Laws, Susan C.</author></authors></contributors><titles><title>Development of a screening approach to detect thyroid disrupting chemicals that inhibit the human sodium iodide symporter (NIS)</title><secondary-title>Toxicology in Vitro</secondary-title></titles><periodical><full-title>Toxicology in Vitro</full-title></periodical><pages>66-78</pages><volume>40</volume><keywords><keyword>Thyroid</keyword><keyword>Endocrine disruptors</keyword><keyword>Sodium iodide symporter</keyword><keyword>Chemical screening</keyword></keywords><dates><year>2017</year><pub-dates><date>4//</date></pub-dates></dates><isbn>0887-2333</isbn><urls><related-urls><url>http://www.sciencedirect.com/science/article/pii/S0887233316302569</url><url>http://ac.els-cdn.com/S0887233316302569/1-s2.0-S0887233316302569-main.pdf?_tid=286edb04-

d8fa-11e6-b2db-

00000aacb360&acdnat=1484248141_9bcc422b76262b7c7843748a566dbb7c</url></related-urls></urls><electronic-resource-num>http://dx.doi.org/10.1016/j.tiv.2016.12.006</electronic-resource-num></record></Cite></EndNote>]. Briefly, 0.35µL of 100µM chemical samples were transferred to assay plate wells containing 69.7µL uptake buffer. Then standards (NaI, 100, 200, 300, 400, 500 nM) were added to specified duplicate wells at 70µL each. To initiate the reaction, 70µL of 24mM sodium arsenite solution and 70µL of 9.9 mM ammonium cerium sulfate solution was added to all wells. The reaction was incubated for 20 minutes at room temperature and subsequently measured for absorbance at 420nm on a SpectraMax Plus Microplate Reader (Molecular Devices, Sunnyvale, CA). Raw A_{420} readings were log10-transformed and NaI standards readings were fitted with linear regression to interpolate iodide concentration for each chemical. All testing was performed in triplicates.

Data analysis

Data analysis was performed in R (ver 3.3.0; R Foundation for Statistical Computing) and documented in R markdown (Supplemental File 1).

Single-concentration screening analysis

RAIU assay raw readings were measured as counts per minute (CPM) and normalized per 96-well plate as the percent activity of the median DMSO control CPM value (n = 12). The median of normalized percent activity from the 3 bioreplicates for each chemical was used to determine whether the chemical would be further evaluated in multi-concentration testing. The activity

threshold was set based on 3 times the baseline median absolute deviation (3bMAD) calculated using DMSO wells from all 15 assay plates in single-concentration screening. As 3bMAD was calculated to be 20.5%, the value for the activity inhibition threshold was rounded to 20% as a more conservative approach for moving chemicals forward to the multi-concentration RAIU and cell viability assays.

Multi-concentration screening analysis

Multi-concentration RAIU assay readings were expressed as CPM and cell viability assay readings were expressed as relative light unit (RLU). Both RAIU and cell viability assay raw readings were normalized using the same method employed in the single-concentration assay.

Dose-response curves were fitted using the Hill model provided in U.S. EPA's ToxCast Pipeline (tcpl v1.2.2) R package [ADDIN EN.CITE <EndNote><Cite><Author>Filer</Author><Year>2017</Year><RecNum>16</RecNum><DisplayText>(Filer<style face="italic"> et al.</style>, 2017)</DisplayText><record><rec-number>16</rec-number><foreign-keys><key app="EN" db-id="09vdaavf8zzsfkefza7x90s6tasptssaefxe" timestamp="1493134067">16</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Filer, Dayne L.</author><author>Kothiya, Parth</author><author>Setzer, R. Woodrow</author><author>Judson, Richard S.</author><author>Martin, Matthew T.</author></authors></contributors><titles><title>tcpl: the ToxCast pipeline for high-throughput screening data</title><secondary-title>Bioinformatics</secondary-title></titles><periodical><full-title>Bioinformatics</full-title></periodical><pages>618-

620</pages><volume>33</volume><number>4</number><dates><year>2017</year></dates>
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urls><url>http://dx.doi.org/10.1093/bioinformatics/btw680</url></related-
urls></urls><electronic-resource-num>10.1093/bioinformatics/btw680</electronic-resource-
num></record></Cite></EndNote>]. The Hill model contains three parameters with bottom asymptote constrained to 0 and is given by the formula:

$$f(x,(tp,ga,gw)) = \frac{tp}{1+10^{(ga-x)gw}}$$

Where x is the log concentration, tp is the top asymptote for the given chemical, ga is the AC_{50} (the log concentration where the modeled activity equals 50% of the top asymptote), and gw is the Hill coefficient. The Hill model provided in the tcpl R package constrains the three parameters as following:

(1) $0 \leq tp \leq 1.2$ times the maximum response value

(2) (minimum log concentration minus 2) $\leq ga \leq$ (maximum log concentration plus 0.5)

(3) $0.3 \leq gw \leq 8$

Prior to curve fitting, the modeling function in the tcpl R package first checked for significant response by comparing the median of normalized chemical responses at each concentration to the 3bMAD value of each assay. The 3bMAD of the multi-concentration RAIU and cell viability assay (23.8% and 17.7% respectively) were calculated separately for each assay using the normalized

response values collected from the two lowest concentrations of all test chemical samples. Curve fitting was only performed when a significant response was present.

Prior to curve fitting, the normalized multi-concentration response data were inversed by using 100 minus the normalized value. This was done because the modeling function in the tcpl R package requires multi-concentration assay data to be conformed in the positive direction, whereas the RAIU and cell viability assay results were in the negative direction (inhibition from maximal response). Predicted response values (yhat) were calculated using the fitted Hill model parameters for each chemical. To visualize assay data and fitted dose-response curve together in the original negative direction, yhat values were subtracted by 100 and used to plot the dose-response curve. The normalized RAIU and cell viability responses, along with their fitted dose-response curve were plotted together in one graph for each chemical using the R package ggplot2 v2.2 [ADDIN EN.CITE

<EndNote><Cite><Author>Wickham</Author><Year>2016</Year><RecNum>70</RecNum><DisplayText>(Wickham, 2016)</DisplayText><record><rec-number>70</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1490799807">70</key></foreign-keys><ref-type name="Book">6</ref-type><contributors><authors><author>Wickham, Hadley</author></authors></contributors><titles><title>ggplot2: elegant graphics for data analysis</title></titles><dates><year>2016</year></dates><publisher>Springer</publisher><isbn>3319242776</isbn><urls></urls></record></Cite></EndNote>].

Calculation of Z', CV of DMSO, AC_{50}, $absEC_{50}$, Cytotox-point

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To monitor the performance of the assay, quality control measures including Z' scores, coefficients of variation (CV) of DMSO, and AC_{50} of positive controls ($NaClO_4$ for RAIU, DCNQ for cell viability) were calculated by each 96-well assay plate. CV of DMSO was calculated by the equation: $CV = SD_{DMSO}/\mu_{DMSO}$, where SD_{DMSO} and μ_{DMSO} are the standard deviation and mean of the raw response value for DMSO control wells, respectively. Z' scores [ADDIN EN.CITE <EndNote><Cite><Author>Zhang</Author><Year>1999</Year><RecNum>65</RecNum><DisplayText>(Zhang<style face="italic"> et al.</style>, 1999)</DisplayText><record><rec-number>65</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1490798592">65</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Zhang, Ji-Hu</author><author>Chung, Thomas D. Y.</author><author>Oldenburg, Kevin R.</author></authors></contributors><titles><title>A Simple Statistical Parameter for Use in Evaluation and Validation of High Throughput Screening Assays</title><secondary-title>Journal of Biomolecular Screening</secondary-title></titles><periodical><full-title>J Biomol Screen</full-title><abbr-1>Journal of biomolecular screening</abbr-1></periodical><pages>67-73</pages><volume>4</volume><number>2</number><dates><year>1999</year><pub-dates><date>1999/04/01</date></pub-dates></dates><publisher>SAGE Publications</publisher><isbn>1087-0571</isbn><urls><related-urls><url>http://journals.sagepub.com/doi/abs/10.1177/108705719900400206</url></related-urls></urls><electronic-resource-num>10.1177/108705719900400206</electronic-resource-num><access-date>2017/02/03</access-date></record></Cite></EndNote>] were calculated as:

$$Z' = 1 - \frac{3(\sigma_{pos} + \sigma_{DMSO})}{|\mu_{pos} - \mu_{DMSO}|}$$

Where σ_{pos} and μ_{pos} are the standard deviation and mean of normalized positive control ($NaClO_4$ for RAIU assay, DCNQ for cell viability assay) values at the highest 100 μM concentration. σ_{DMSO} and μ_{DMSO} are the standard deviation and mean of normalized DMSO control values. AC_{50} (the log concentration where the modeled activity equals 50% of the chemical's modeled maximal activity) was reported for all chemicals with fitted dose-response curves. For chemicals that inhibited iodide uptake by > 50%, absolute EC_{50} ($absEC_{50}$) were also reported. $absEC_{50}$ was determined as the log concentration where the modeled activity equals 50% of control activity. absEC80 was determined as the log concentration where the modeled activity equals 80% of control activity.

For chemicals that demonstrated significant cytotoxicity (exceeding 3bMAD of cell viability assay, 17.7%), the concentration where a significant reduction in cell viability for each chemical was determined and referred to as the cytotox-point. Cytotox-point is the equivalent of $absEC_{82.3}$, the log concentration where the modelled activity equals the significant cytotoxicity cutoff value (82.3% of control viability).

Chemical ranking score

To prioritize the chemicals for potential NIS inhibition activity, a new ranking system was developed based on two metrics that take into account the confounding impact of cytotoxicity on identifying RAIU inhibition activity: 1) toxicity-adjusted area (TAA) and 2) the difference of median responses of RAIU and cytotoxicity at maximum tested concentration (Median-Difference)

(Fig. 1). Ranking analysis was only performed if a chemical produced significant RAIU inhibition in multi-concentration screening. To obtain TAA (gray stripe area illustrated in Fig.1), RAIU inhibition area and cytotoxicity area were first calculated. RAIU inhibition area was defined by the RAIU 3bMAD (23.8%) significant threshold horizontal line (top border), maximum concentration vertical line (right border), and the RAIU dose-response curve. Cytotoxicity area was defined with the same top and right borders and the cell viability dose-response curve. TAA was then obtained by subtracting the cytotoxicity area from the RAIU inhibition area. Therefore, the numeric value of TAA is penalized when a chemical demonstrates strong cytotoxicity. Median-Difference was calculated using the median of cell viability responses minus the median of RAIU responses at the maximum tested concentration (usually 100 μM). Larger Median-Difference values represent larger separations between RAIU and cytotoxicity.

To rank test chemicals, the well-known NIS inhibitor $NaClO_4$ was chosen as the reference chemical to normalize the TAA and Median-Difference of each test chemical. Specifically, the TAA and Median-Difference values of $NaClO_4$ positive control included on each of the 54 multi-concentration testing plates were first calculated to obtain the median of $NaClO_4$ TAA and Median-Difference (150.03 and 95.67 respectively). The TAA and Median-Difference of test chemicals were normalized as the percentage of the median $NaClO_4$ TAA and Median-Difference separately and then summed to obtain a chemical ranking score. The ranking score of 200 represents the potency of the reference $NaClO_4$ (Fig. 1A). Fig. 1B, 1C and 1D show the dose-response of three test chemicals with lower level of ranking scores due to less RAIU inhibition and increased cytotoxicity level.

[PAGE * MERGEFORMAT]

Results

Single-concentration screening

To facilitate the screening process, the 310 blinded samples were first tested in the RAIU assay at their maximum permissible concentration (typically at 100 μM, Table 2) to select potentially active compounds for concentration-response evaluation. Assay performance of single-concentration screening was monitored for each assay plate (total number of plates = 15) through CV of DMSO vehicle control, Z' and AC_{50} for the positive control chemical $NaClO_4$ (Table 3). The CV of DMSO control wells for each plate ranged from 4.91% to 11.04%, with mean ± SD of 7.14% ± 1.56%. Z' scores ranged from 0.65 to 0.84, with mean ± SD of 0.77 ± 0.05. AC_{50} (logM) of $NaClO_4$ ranged from -6.56 to -6.06, with mean ± SD of -6.44 ± 0.11. In addition, the responses of control chemicals included on each assay plate are summarized for the entire screening campaign in Table 4. The DMSO (vehicle control), 2,4-D (negative control), $NaNO_3$ (EC_{80} positive control), NaSCN (EC_{20} positive control) achieved mean ± SD of 100.63% ± 7.11%, 92.41% ± 4.24%, 81.25% ± 7.56%, 20.64% ± 1.12%, respectively. Overall, these metrics indicate the RAIU assay in single-concentration screening performed well with sufficient dynamic range, reproducibility, and reliability.

Single-concentration RAIU screening results for all 310 samples were ordered by increasing inhibitory median responses and plotted as median and maximum/minimum responses for each sample (Fig.2). These samples demonstrated a wide range of iodide uptake inhibition activity in the assay with median responses ranging from 2.8% to 116.6% of maximum iodide uptake relative

to DMSO control. Of the 310 samples, 169 samples (54.5%) produced over the pre-determined 20% inhibition threshold and were selected for multi-concentration testing (Table 2).

Blinded internal replicate chemicals

The phase I_v2 chemical library consisted of 310 blinded samples that included 293 unique chemicals. Twelve of these chemicals were internally replicated (7 chemicals replicated twice and 5 chemicals replicated three times) to assess assay reproducibility. The robustness of the RAIU assay is shown in Fig. 3a, where all 12 replicated chemicals, excepting bisphenol A, produced highly reproducible results. Of the 12 replicated chemicals, 10 exceeded the 20% inhibition threshold and were subsequently tested in multi-concentration screening. The AC_{50} for each replicate of the 10 chemicals was calculated to assess the reproducibility of the RAIU assay in the multi-concentration setting (Fig. 3b, Supplemental Table 1). These 10 internal replicate samples had highly reproducible AC_{50} (logM) values with the maximum range of variation less than 0.25 (logM).

Multi-concentration testing

The 169 blinded samples with ≥20% inhibition in single-concentration RAIU screening were retested at 6 concentrations (0.001μM – 100μM) in parallel RAIU and cell viability assays. Both RAIU and cell viability assays performed reliably and their performance metrics calculated by each assay plate (total number of plates = 54) are summarized in Table 3. The CV of DMSO controls for RAIU and cell viability assays had mean ± SD of 8.61% ± 1.01%, 5.42% ± 1.47%, respectively. The Z' for the RAIU assay had a range of 0.64 - 0.78 and mean ± SD of 0.72 ± 0.03.

The AC_{50} (logM) of positive controls ($NaClO_4$ for the RAIU assay, DCNQ for the cell viability assay) also demonstrated high reproducibility across assay plates, with mean ± SD of -6.38 ± 0.13, -4.83 ± 0.12 for RAIU and cell viability assays, respectively. The dose-response curves of $NaClO_4$ and DCNQ positive controls in multi-concentration screening are provided in Supplemental Figure 3. Additionally, the responses of all control chemicals are summarized across all assay plates in Table 4. All controls of the RAIU and cell viability assays showed great consistency with small variances in multi-concentration testing. The DMSO (vehicle control), 2,4-D (RAIU negative control), $NaNO_3$ (RAIU EC_{80} positive control), and NaSCN (RAIU EC_{20} positive control) achieved mean ± SD of 99.5% ± 8.28%, 90.86% ± 4.49%, 83.08% ± 7.17%, and 24.69% ± 2.71% respectively in RAIU assay. In the cell viability assay, DMSO, 2,4-D, $NaNO_3$, and NaSCN were inactive, with responses (mean±SD) of 100.92% ± 5.41%, 99.34% ± 3.21%, 98.95% ± 5.43%, and 104.3% ± 3.98%, respectively.

The significant activity threshold (3bMAD, calculated across all 54 assay plates in multi-concentration screening) for cell viability and RAIU assays were 17.7% and 23.8%, respectively. Among the 169 tested samples, 137 showed significant RAIU inhibition activity (>23.8% inhibition) and 127 exhibited significant cytotoxicity (>17.7% inhibition). Within the 137 samples with significant RAIU inhibition activity, 111 displayed a cytotoxic response while no change in cell viability was observed in 26 samples. There were 16 chemicals that caused significant cytotoxicity with no significant RAIU inhibition.

In reporting the RAIU and cell viability responses of each test chemical, several activity metrics, including AC_{50}, $absEC_{50}$, and cytotox-point (Table 2) were used together to aid in the interpretation of the assay results. AC_{50} and $absEC_{50}$ indicate the chemical potency from two different perspectives, as they differ in the inhibition activity level each represents. $absEC_{50}$ is the concentration that causes 50% inhibition, while AC_{50} is the concentration that triggers half-maximal inhibition, which is <50% inhibition for chemicals that do not fully inhibit NIS activity at the maximal concentration tested. AC_{50} is a useful metric to rank potencies even if the test chemical has low efficacy, provided that an activity curve can be fit. However, AC_{50} is not suitable to compare chemicals with different maximum inhibition activities, as their AC_{50} values represent the effective concentrations at different absolute activity levels. Moreover, the AC_{50} value of any given chemical may shift if it can produce stronger inhibition at higher test concentrations. To avoid these two issues, $absEC_{50}$ was calculated and reported. A reported $absEC_{50}$ value also indicates that the chemical exhibited ≥50% inhibition in the RAIU assay. For quick reference of the occurrence of cytotoxicity, the cytotox-point, which represents the concentration where significant cytotoxicity was observed, was reported along with the AC_{50} and $absEC_{50}$ values. Dose-response curves for each chemical are available in Supplemental Figure 2. AC50 and absEC50 values for cell viability assay are provided in Supplemental Table 2.

When comparing results from the highest concentration in multi-concentration screening and single-concentration screening, 87% of the chemicals (147 of 169) tested in multi-concentration format produced over 20% inhibition in RAIU assay, the significance threshold chosen for the single-concentration screening. Twenty-two chemicals failed to meet the 20% inhibition threshold

during multi-concentration testing. The range of their median RAIU inhibition in the initial single-concentration screen was between 20.9% to 51.8%, and 14 of the 22 chemicals had a median inhibition below 30%, indicating that these chemicals were weak actives in the initial single-concentration screen.

Chemical potency ranking

To prioritize chemicals for further analysis, the 169 samples tested in multi-concentration were further analyzed by a newly developed ranking system that estimates the RAIU inhibitory potency while mitigating the negative impact of cytotoxicity on identifying RAIU activity (Fig. 1). Of the 169 chemical samples tested in multi-concentration, 32 did not produce significant RAIU inhibition and hence were excluded in the ranking analysis. The ranking scores of the 137 chemical samples are listed and illustrated in Table 2 and Fig. 4. The TAA and Median-Difference values for these chemicals are provided in Supplemental Table 2.

In this study, the reference chemical $NaClO_4$ exhibited the most potent RAIU inhibition with a ranking score of 200 (both TAA and Median-Difference valued at 100). In comparison, the ranking score of the 137 test chemical samples ranged from 150.41 to -29.52, with 4 having ranking scores >100, 17 having ranking scores between 50 and 100, and 116 having ranking scores <50. An overview of the cytotoxicity of the ranked chemicals at the maximum concentration tested is shown in Fig. 4. Of the 137 chemical samples that produced significant RAIU inhibition, 27 exhibited no cytotoxicity, 67 exhibited significant but <50% cytotoxicity, and 43 exhibited >50% cytotoxicity at the maximum concentration.

The dose-response curves along with the ranking score, AC_{50} and $absEC_{50}$ for the first 15 ranked samples (14 chemicals) are shown in Fig. 5a. These 15 samples have ranking score ranged from 150.41 to 64.10, AC50 ranged from -4.33 to -8.64, absEC50 ranged from -4.37 to -7.49. Fig. 5b shows three examples of the 32 chemicals that failed to produce significant RAIU inhibition, with either no significant or nominal cytotoxicity.

Identification of Iodide interference

The 310 samples were also tested with SK reactions to determine the presence of any contaminant iodide that may lead to potential false positive RAIU inhibition. Only two chemicals (iodosulfuron-methyl-sodium and 3-iodo-2-propynyl-N-butylcarbamate) produced positive SK reactions, suggesting that overall iodide contamination was not introducing false positive results in the RAIU assay. Iodosulfuron-methyl-sodium produced a positive SK reaction with interpolated content of 12.69 ± 1.12 pmol/well of equivalent I^-. However, this chemical had <20% RAIU inhibition in the single-concentration screening and therefore was not tested in the multi-concentration assay. 3-iodo-2-propynyl-N-butylcarbamate produced A_{420} readings beyond the upper range of the standard curve (> 35pmol/well). However, since 3-iodo-2-propynyl-N-butylcarbamate structurally contains iodide, it is unclear whether the strong S-K reaction was triggered by the chemical itself or the iodide contamination in the sample. This uncertainty about iodide contamination confounds any intrepetation of 3-iodo-2-propynyl-N-butylcarbamate results as an efficaious NIS inhibitor in the RAIU assay.

Discussion

This study represents the first large-scale screening effort to identify potential NIS inhibitors in an environmental chemical library using our previously developed HTS approach [ADDIN EN.CITE <EndNote><Cite><Author>Hallinger</Author><Year>2017</Year><RecNum>64</RecNum><DisplayText>(Hallinger<style face="italic"> et al.</style>, 2017)</DisplayText><record><rec-number>64</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1490798592">64</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Hallinger, Daniel R.</author><author>Murr, Ashley S.</author><author>Buckalew, Angela R.</author><author>Simmons, Steven O.</author><author>Stoker, Tammy E.</author><author>Laws, Susan C.</author></authors></contributors><titles><title>Development of a screening approach to detect thyroid disrupting chemicals that inhibit the human sodium iodide symporter (NIS)</title><secondary-title>Toxicology in Vitro</secondary-title></titles><periodical><full-title>Toxicology in Vitro</full-title></periodical><pages>66-78</pages><volume>40</volume><keywords><keyword>Thyroid</keyword><keyword>Endocrine disruptors</keyword><keyword>Sodium iodide symporter</keyword><keyword>Chemical screening</keyword></keywords><dates><year>2017</year><pub-dates><date>4//</date></pub-dates></dates><isbn>0887-2333</isbn><urls><related-urls><url>http://www.sciencedirect.com/science/article/pii/S0887233316302569</url><url>http

://ac.els-cdn.com/S0887233316302569/1-s2.0-S0887233316302569-main.pdf?_tid=286edb04-d8fa-11e6-b2db-00000aacb360&acdnat=1484248141_9bcc422b76262b7c7843748a566dbb7c</url></related-urls></urls><electronic-resource-num>http://dx.doi.org/10.1016/j.tiv.2016.12.006</electronic-resource-num></record></Cite></EndNote>]. The results demonstrate that this assay performed with high reproducibility and reliability as measured by typical performance metrics for HTS assays. The assay demonstrated a high Z' score and low variability in DMSO vehicle controls in both the single- and multi-concentration RAIU screenings. The internal chemical replicates, included for quality control purposes, also demonstrated consistent responses that further support strong assay reproducibility.

Prioritizing chemical RAIU inhibition potency based on a cell-based assay can be confounded if the test compound exhibits strong cytotoxicity. Therefore, a great effort was made to conduct a parallel cell viability assay using the same batch of cell culture, the same treatment and experimental conditions with the RAIU assay to provide the best possible estimation of cytotoxicity. To maximize the usage of the rigorous cytotoxicity data, a novel potency ranking system was developed to prioritize potential NIS inhibitors. Based on both RAIU and cytotoxicity dose-responses, this system adapts cytotoxicity in calculating the two underlying metrics, TAA and Median-Difference. The ranking score was also normalized in reference to the well-known NIS inhibitor sodium perchlorate, making it compatible for comparisons with chemicals in future screenings. Overall, this ranking system enhances the quality of chemical prioritization when compared to other systems that rely on single point metrics. With this ranking system, the top

ranked 15 samples (Fig. 5a) represent a diverse group of 14 environmental chemicals with different known toxicological properties and are further discussed below.

Several of these highly ranked chemicals are pesticides that showed potential effects on cellular energy. For example, etoxazole is an organofluorine acaricide-insecticide and was the highest ranked among all the tested chemicals, with a typical sigmoidal RAIU inhibition response and minimal cytotoxicity (25.2% median inhibition) at the highest test concentration. The U.S. EPA ToxRef database [ADDIN EN.CITE <EndNote><Cite><Author>Martin</Author><Year>2009</Year><RecNum>59</RecNum><DisplayText>(Martin<style face="italic"> et al.</style>, 2009)</DisplayText><record><rec-number>59</rec-number><foreign-keys><key app="EN" db-id="09vdaavf8zzsfkefza7x90s6tasptssaefxe" timestamp="1499258815">59</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Martin, MT</author><author>Judson, RS</author><author>Reif, DM</author><author>Kavlock, RJ</author><author>Dix, DJ</author></authors></contributors><titles><title>Profiling chemicals based on chronic toxicity results from the US EPA ToxRef Database</title><secondary-title>Environmental Health Perspectives</secondary-title></titles><periodical><full-title>Environmental Health Perspectives</full-title></periodical><pages>392-399</pages><volume>117</volume><number>3</number><dates><year>2009</year></dates><isbn>0091-6765</isbn><urls></urls></record></Cite></EndNote>], a collection of curated *in vivo* regulatory toxicity information previously submitted to the agency, reveals that etoxazole can lead to increase of thyroid gland weight in both subchronic and chronic rat oral toxicity studies.

Our finding is the first to show that etoxazole disrupts iodide uptake by NIS. However, whether etoxazole can directly interact with the NIS protein requires further investigation, as a study on the freshwater fish *Oreochromis niloticus* found that etoxazole exposure at high concentration can lead to increase of Na^+/K^+ ATPase activities in gill and muscle and a decrease of this activity in kidney [ADDIN EN.CITE <EndNote><Cite><Author>Üner</Author><Year>2005</Year><RecNum>42</RecNum><DisplayText>(Üner<style face="italic"> et al.</style>, 2005)</DisplayText><record><rec-number>42</rec-number><foreign-keys><key app="EN" db-id="09vdaavf8zzsfkefza7x90s6tasptssaefxe" timestamp="1496349898">42</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Üner, Nevin</author><author>Oruç, Elif</author><author>Sevgiler, Yusuf</author></authors></contributors><titles><title>Oxidative stress-related and ATPase effects of etoxazole in different tissues of Oreochromis niloticus</title><secondary-title>Environmental Toxicology and Pharmacology</secondary-title></titles><periodical><full-title>Environmental Toxicology and Pharmacology</full-title></periodical><pages>99-106</pages><volume>20</volume><number>1</number><keywords><keyword>Etoxazole</keyword><keyword>Antioxidant enzyme</keyword><keyword>Oxidative stress</keyword><keyword>Lipid peroxidation</keyword><keyword>ATPase</keyword><keyword>Fish tissues</keyword></keywords><dates><year>2005</year><pub-dates><date>7//</date></pub-dates></dates><isbn>1382-6689</isbn><urls><related-urls><url>http://www.sciencedirect.com/science/article/pii/S1382668904002418</url><url>http

://ac.els-cdn.com/S1382668904002418/1-s2.0-S1382668904002418-main.pdf?_tid=2d359ba4-39a4-11e7-8f97-00000aab0f26&acdnat=1494876475_48b693815708540978a9cf4a54820f14</url></related-urls></urls><electronic-resource-num>https://doi.org/10.1016/j.etap.2004.11.006</electronic-resource-num></record></Cite></EndNote>]. Since Na^+/K^+ ATPase maintains the critical cross-membrane sodium gradient necessary for NIS functionality, disruption of Na^+/K^+ ATPase activity can indirectly affect NIS activity. Another high-ranking chemical, niclosamide, may also have interfered with NIS function indirectly, as it is a pharmaceutical that uncouples oxidative phosphorylation in mitochondria [ADDIN EN.CITE <EndNote><Cite><Author>Pearson</Author><Year>1985</Year><RecNum>43</RecNum><DisplayText>(Pearson and Hewlett, 1985)</DisplayText><record><rec-number>43</rec-number><foreign-keys><key app="EN" db-id="09vdaavf8zzsfkefza7x90s6tasptssaefxe" timestamp="1496349898">43</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Pearson, R. D.</author><author>Hewlett, E. L.</author></authors></contributors><titles><title>NIclosamide therapy for tapeworm infections</title><secondary-title>Annals of Internal Medicine</secondary-title></titles><periodical><full-title>Annals of Internal Medicine</full-title></periodical><pages>550-551</pages><volume>102</volume><number>4</number><dates><year>1985</year></dates><isbn>0003-4819</isbn><urls><related-urls><url>http://dx.doi.org/10.7326/0003-4819-102-4-550</url></related-urls></urls><electronic-resource-num>10.7326/0003-4819-102-4-550</electronic-resource-num></record></Cite></EndNote>], thereby disrupt ATP production

and hence Na^+/K^+ ATPase activity. To date, there is no report of niclosamide regarding thyroid toxicity, except its anti-proliferative effect in human thyroid cancer cells [ADDIN EN.CITE <EndNote><Cite><Author>Zhang</Author><Year>2012</Year><RecNum>44</RecNum><DisplayText>(Zhang<style face="italic"> et al.</style>, 2012)</DisplayText><record><rec-number>44</rec-number><foreign-keys><key app="EN" db-id="09vdaavf8zzsfkefza7x90s6tasptssaefxe" timestamp="1496349899">44</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Zhang, Lisa</author><author>He, Mei</author><author>Zhang, Yaqin</author><author>Nilubol, Naris</author><author>Shen, Min</author><author>Kebebew, Electron</author></authors></contributors><titles><title>Quantitative High-Throughput Drug Screening Identifies Novel Classes of Drugs with Anticancer Activity in Thyroid Cancer Cells: Opportunities for Repurposing</title><secondary-title>The Journal of Clinical Endocrinology & Metabolism</secondary-title></titles><periodical><full-title>The Journal of Clinical Endocrinology & Metabolism</full-title></periodical><pages>E319-E328</pages><volume>97</volume><number>3</number><dates><year>2012</year></dates><isbn>0021-972X</isbn><urls><related-urls><url>http://dx.doi.org/10.1210/jc.2011-2671</url></related-urls></urls><electronic-resource-num>10.1210/jc.2011-2671</electronic-resource-num></record></Cite></EndNote>].

Several other insecticides in this study have been shown to disrupt energy metabolism and demonstrated similar atypical RAIU dose-response curves that may implicate an alternative mechanism of NIS inhibition. These chemicals include rotenone and pyridaben (Fig. 5a), which

are both mitochondrial complex I inhibitors that disrupt electron transport leading to reduced ATP production [ADDIN EN.CITE <EndNote><Cite><Author>Hollingworth</Author><Year>1994</Year><RecNum>102</RecNum><DisplayText>(Hollingworth<style face="italic"> et al.</style>, 1994)</DisplayText><record><rec-number>102</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1496174640">102</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Hollingworth, R. M.</author><author>Ahammadsahib, K. I.</author><author>Gadelhak, G.</author><author>McLaughlin, J. L.</author></authors></contributors><auth-address>PURDUE UNIV,DEPT MED CHEM & PHARMACOGNOSY,W LAFAYETTE,IN 47907.
HOLLINGWORTH, RM (reprint author), MICHIGAN STATE UNIV,PESTICIDE RES CTR,E LANSING,MI 48824, USA.</auth-address><titles><title>NEW INHIBITORS OF COMPLEX-I OF THE MITOCHONDRIAL ELECTRON-TRANSPORT CHAIN WITH ACTIVITY AS PESTICIDES</title><secondary-title>Biochemical Society Transactions</secondary-title><alt-title>Biochem. Soc. Trans.</alt-title></titles><periodical><full-title>Biochemical Society Transactions</full-title><abbr-1>Biochem. Soc. Trans.</abbr-1></periodical><alt-periodical><full-title>Biochemical Society Transactions</full-title><abbr-1>Biochem. Soc. Trans.</abbr-1></alt-periodical><pages>230-233</pages><volume>22</volume><number>1</number><keywords><keyword>NADH DEHYDROGENASE</keyword><keyword>REDUCTASE</keyword><keyword>ROTENONE</keyword><keyword>Biochemistry & Molecular

Biology</keyword></keywords><dates><year>1994</year><pub-dates><date>Feb</date></pub-dates></dates><isbn>0300-5127</isbn><accession-num>WOS:A1994NA92900049</accession-num><work-type>Article; Proceedings Paper</work-type><urls><related-urls><url><Go to ISI>://WOS:A1994NA92900049</url></related-urls></urls><language>English</language></record></Cite></EndNote>]. Rotenone has been shown to inhibit iodide uptake in sheep thyroid slices [ADDIN EN.CITE <EndNote><Cite><Author>Tyler</Author><Year>1968</Year><RecNum>100</RecNum><DisplayText>(Tyler<style face="italic"> et al.</style>, 1968)</DisplayText><record><rec-number>100</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1496172914">100</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Tyler, D D</author><author>Gonze, Jeanine</author><author>Lamy, Françoise</author><author>Dumont, J. E.</author></authors></contributors><titles><title>Influence of mitochondrial inhibitors on the respiration and energy-dependent uptake of iodide by thyroid slices</title><secondary-title>Biochemical Journal</secondary-title></titles><periodical><full-title>Biochemical Journal</full-title></periodical><pages>123-133</pages><volume>106</volume><number>1</number><dates><year>1968</year></dates><urls></urls><electronic-resource-num>10.1042/bj1060123</electronic-resource-num></record></Cite></EndNote>] and pyridaben has been associated to reduced thyroid gland weight in subchronic rat study according to U.S.EPA ToxRef database [ADDIN EN.CITE

<EndNote><Cite><Author>Martin</Author><Year>2009</Year><RecNum>59</RecNum><DisplayText>(Martin<style face="italic"> et al.</style>, 2009)</DisplayText><record><rec-number>59</rec-number><foreign-keys><key app="EN" db-id="09vdaavf8zzsfkefza7x90s6tasptssaefxe" timestamp="1499258815">59</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Martin, MT</author><author>Judson, RS</author><author>Reif, DM</author><author>Kavlock, RJ</author><author>Dix, DJ</author></authors></contributors><titles><title>Profiling chemicals based on chronic toxicity results from the US EPA ToxRef Database</title><secondary-title>Environmental Health Perspectives</secondary-title></titles><periodical><full-title>Environmental Health Perspectives</full-title></periodical><pages>392-399</pages><volume>117</volume><number>3</number><dates><year>2009</year></dates><isbn>0091-6765</isbn><urls></urls></record></Cite></EndNote>]. Several lower ranked chemicals (Supplemental Fig. 2) including fenpyroximate, tebufenpyrad (mitochondrial NADH-CoQ reductase inhibitor), and pyraclostrobin (quinone inhibitor) may also disrupt energy levels [ADDIN EN.CITE ADDIN EN.CITE.DATA]. These chemicals have similar atypical dose-responses in the RAIU assay with a very flat slope and they all produced significant effects on cell viability. Since the Cell-Titer Glo viability assay quantifies ATP as an indicator of viable cells, this effect on cell viability could be the result of either energy metabolism disruption or cell death. A secondary cell viability assay using an alternative indicator of viability can confirm the cytotoxicity observed.

Several chemicals in the top 14 chemicals, including PFOS, triphenyltin hydroxide, and fipronil have been shown to disrupt thyroid function in previous studies and had significant effects on iodide uptake by NIS in the current study. Among these three chemicals, PFOS has been the most studied due to its widespread presence and persistence in the environment. PFOS was reported to decrease serum T4 levels in mammalian models such as the rat, mouse, and monkey [ADDIN EN.CITE ADDIN EN.CITE.DATA]. Aquatic exposure to PFOS has also been shown to increase T3 level, upregulate NIS expression, and alter expression of other HPT genes in zebrafish larvae [ADDIN EN.CITE <EndNote><Cite><Author>Shi</Author><Year>2009</Year><RecNum>53</RecNum><DisplayText>(Shi<style face="italic"> et al.</style>, 2009)</DisplayText><record><rec-number>53</rec-number><foreign-keys><key app="EN" db-id="09vdaavf8zzsfkefza7x90s6tasptssaefxe" timestamp="1496349899">53</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Shi, Xiongjie</author><author>Liu, Chunsheng</author><author>Wu, Guoqiao</author><author>Zhou, Bingsheng</author></authors></contributors><titles><title>Waterborne exposure to PFOS causes disruption of the hypothalamus–pituitary–thyroid axis in zebrafish larvae</title><secondary-title>Chemosphere</secondary-title></titles><periodical><full-title>Chemosphere</full-title></periodical><pages>1010-1018</pages><volume>77</volume><number>7</number><keywords><keyword>PFOS</keyword><keyword>Hypothalamic–pituitary–thyroid axis</keyword><keyword>Thyroid hormone</keyword><keyword>Zebrafish</keyword></keywords><dates><year>2009</year><

pub-dates><date>11//</date></pub-dates></dates><isbn>0045-6535</isbn><urls><related-urls><url>http://www.sciencedirect.com/science/article/pii/S0045653509009126</url></related-urls></urls><electronic-resource-num>https://doi.org/10.1016/j.chemosphere.2009.07.074</electronic-resource-num></record></Cite></EndNote>]. In addition, higher concentrations of serum PFOA and PFOS have been associated with current thyroid disease in the U.S. general adult population [ADDIN EN.CITE <EndNote><Cite><Author>Melzer</Author><Year>2010</Year><RecNum>54</RecNum><DisplayText>(Melzer<style face="italic"> et al.</style>, 2010)</DisplayText><record><rec-number>54</rec-number><foreign-keys><key app="EN" db-id="09vdaavf8zzsfkefza7x90s6tasptssaefxe" timestamp="1496349899">54</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Melzer, David</author><author>Rice, Neil</author><author>Depledge, Michael H.</author><author>Henley, William E.</author><author>Galloway, Tamara S.</author></authors></contributors><titles><title>Association between Serum Perfluorooctanoic Acid (PFOA) and Thyroid Disease in the U.S. National Health and Nutrition Examination Survey</title><secondary-title>Environmental Health Perspectives</secondary-title></titles><periodical><full-title>Environmental Health Perspectives</full-title></periodical><pages>686-692</pages><volume>118</volume><number>5</number><dates><year>2010</year><pub-dates><date>01/20
10/17/received
01/07/accepted</date></pub-dates></dates><publisher>National Institute of Environmental Health

Sciences</publisher><isbn>0091-6765
1552-9924</isbn><accession-num>PMC2866686</accession-num><urls><related-urls><url>http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2866686/</url></related-urls></urls><electronic-resource-num>10.1289/ehp.0901584</electronic-resource-num><remote-database-name>PMC</remote-database-name></record></Cite></EndNote>]. In this study, the two PFOS samples (internally replicated in ToxCast library) both produced significant RAIU inhibition with similar dose-responses (Fig. 6a). The absEC$_{50}$ values for the two PFOS samples were also very close with values of -4.78 and -4.74 (logM), respectively. Triphenyltin hydroxide is a fungicide that has been shown to impair reproduction in rats and cause reduced pituitary, thyroid weight, and increased incidence of pituitary tumors [ADDIN EN.CITE <EndNote><Cite><Author>Golub</Author><Year>2004</Year><RecNum>55</RecNum><DisplayText>(Golub and Doherty, 2004)</DisplayText><record><rec-number>55</rec-number><foreign-keys><key app="EN" db-id="09vdaavf8zzsfkefza7x90s6tasptssaefxe" timestamp="1496349899">55</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Golub, Mari S</author><author>Doherty, John D</author></authors></contributors><titles><title>Triphenyltin as a potential human endocrine disruptor</title><secondary-title>Journal of Toxicology and Environmental Health, Part B</secondary-title></titles><periodical><full-title>Journal of Toxicology and Environmental Health, Part B</full-title></periodical><pages>281-295</pages><volume>7</volume><number>4</number><dates><year>2004</year></dates><isbn>1093-7404</isbn><urls></urls></record></Cite></EndNote>]. A study with Japanese quail also reported decreased serum T4 level and impaired reproduction following triphenyltin

hydroxide dietary exposure [ADDIN EN.CITE <EndNote><Cite><Author>Grote</Author><Year>2006</Year><RecNum>56</RecNum><DisplayText>(Grote<style face="italic"> et al.</style>, 2006)</DisplayText><record><rec-number>56</rec-number><foreign-keys><key app="EN" db-id="09vdaavf8zzsfkefza7x90s6tasptssaefxe" timestamp="1496349899">56</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Grote, K.</author><author>Niemann, L.</author><author>Gericke, C.</author><author>Selzsam, B.</author><author>Chahoud, I.</author></authors></contributors><titles><title>Effects of fentin hydroxide on reproduction of the Japanese quail (Coturnix coturnix japonica)</title><secondary-title>Environmental Research</secondary-title></titles><periodical><full-title>Environmental Research</full-title></periodical><pages>81-88</pages><volume>101</volume><number>1</number><keywords><keyword>Fentin hydroxide</keyword><keyword>Organotin compounds</keyword><keyword>Japanese quail</keyword><keyword>Reproduction</keyword><keyword>Endorine disruption</keyword></keywords><dates><year>2006</year><pub-dates><date>5//</date></pub-dates></dates><isbn>0013-9351</isbn><urls><related-urls><url>http://www.sciencedirect.com/science/article/pii/S0013935105001015</url></related-urls></urls><electronic-resource-num>https://doi.org/10.1016/j.envres.2005.07.004</electronic-resource-num></record></Cite></EndNote>]. In our study, triphenyltin hydroxide demonstrated a typical RAIU inhibition dose-response (absEC50 = -5.39 logM) with moderate cytotoxicity only at 100 μM. Fipronil is a broadly used insecticide that has been associated with elevated rates of T4

elimination in the rat and increased hepatic enzyme activity was suggested to be the cause [ADDIN EN.CITE <EndNote><Cite><Author>Leghait</Author><Year>2009</Year><RecNum>57</RecNum><DisplayText>(Leghait<style face="italic"> et al.</style>, 2009)</DisplayText><record><rec-number>57</rec-number><foreign-keys><key app="EN" db-id="09vdaavf8zzsfkefza7x90s6tasptssaefxe" timestamp="1496349900">57</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Leghait, Julien</author><author>Gayrard, Véronique</author><author>Picard-Hagen, Nicole</author><author>Camp, Marion</author><author>Perdu, Elisabeth</author><author>Toutain, Pierre-Louis</author><author>Viguié, Catherine</author></authors></contributors><titles><title>Fipronil-induced disruption of thyroid function in rats is mediated by increased total and free thyroxine clearances concomitantly to increased activity of hepatic enzymes</title><secondary-title>Toxicology</secondary-title></titles><periodical><full-title>Toxicology</full-title></periodical><pages>38-44</pages><volume>255</volume><number>1–2</number><keywords><keyword>Thyroid disruptor</keyword><keyword>Rat</keyword><keyword>Clearance</keyword><keyword>UDPGT</keyword><keyword>Fipronil</keyword><keyword>5-Amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-(trifluoromethylsulfinyl)-1H-pyrazole-3-carbonitrile</keyword></keywords><dates><year>2009</year><pub-dates><date>1/8/</date></pub-dates></dates><isbn>0300-483X</isbn><urls><related-urls><url>http://www.sciencedirect.com/science/article/pii/S0300483X08004654</url></related-urls></urls><electronic-resource-num>https://doi.org/10.1016/j.tox.2008.09.026</electronic-

resource-num></record></Cite></EndNote>]. The same group later conducted a fipronil study in sheep and found that the thyroid disruption activity previously observed in the rat could not be replicated in rams, and only a moderate level of increased T4 clearance was observed in ewes [ADDIN EN.CITE <EndNote><Cite><Author>Leghait</Author><Year>2010</Year><RecNum>58</RecNum><DisplayText>(Leghait<style face="italic"> et al.</style>, 2010)</DisplayText><record><rec-number>58</rec-number><foreign-keys><key app="EN" db-id="09vdaavf8zzsfkefza7x90s6tasptssaefxe" timestamp="1496349900">58</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Leghait, Julien</author><author>Gayrard, Véronique</author><author>Toutain, Pierre-Louis</author><author>Picard-Hagen, Nicole</author><author>Viguié, Catherine</author></authors></contributors><titles><title>Is the mechanisms of fipronil-induced thyroid disruption specific of the rat: Re-evaluation of fipronil thyroid toxicity in sheep?</title><secondary-title>Toxicology Letters</secondary-title></titles><periodical><full-title>Toxicology Letters</full-title></periodical><pages>51-57</pages><volume>194</volume><number>3</number><keywords><keyword>Fipronil</keyword><keyword>Thyroid toxicicity</keyword><keyword>Endocrine disruptor</keyword><keyword>Toxicokinetic</keyword><keyword>Sheep</keyword></keywords><dates><year>2010</year><pub-dates><date>5/4/</date></pub-dates></dates><isbn>0378-4274</isbn><urls><related-urls><url>http://www.sciencedirect.com/science/article/pii/S0378427410000329</url></related-urls></urls><electronic-resource-num>https://doi.org/10.1016/j.toxlet.2010.01.018</electronic-

resource-num></record></Cite></EndNote>]. In our study, fipronil demonstrated significant RAIU inhibition between 10 μM and 100 μM and significant cytotoxicity at 100 μM.

Apart from the chemicals discussed above, five of the top 14 chemicals were only associated with thyroid disruption activity in the U.S.EPA ToxRef database but no other published literature. The records in ToxRef database indicate that 3-iodo-2-propynyl-N-butylcarbamate, cyprodinil, and methoxyfenozide were associated with pathological changes in thyroid gland in subchronic rat toxicity studies. Cyprodinil also caused increased thyroid gland weight. ToxRef database also has records for captan and oxyfluorfen reporting increased thyroid gland weight in chronic rat toxicity studies. However, record usability in ToxRef for captan and oxyfluorfen was labaled as "deficient evaluation" and "unacceptable", respectively. Hence, these results may be unreliable. Fluroxypyr-meptyl and 2-(thiocyanomethylthio)benzothiazole were not previously associated with thyroid disruption, though similarly structured benzothiozoles have previously been identified as thyroid peroxidase inhibitors [ADDIN EN.CITE <EndNote><Cite><Author>Hornung</Author><Year>2015</Year><RecNum>91</RecNum><DisplayText>(Hornung<style face="italic"> et al.</style>, 2015)</DisplayText><record><rec-number>91</rec-number><foreign-keys><key app="EN" db-id="tsarvxesktrfvwe9d9rxsxthda0dev5r55ef" timestamp="1494528450">91</key></foreign-keys><ref-type name="Journal Article">17</ref-type><contributors><authors><author>Hornung, Michael W.</author><author>Kosian, Patricia A.</author><author>Haselman, Jonathan T.</author><author>Korte, Joseph J.</author><author>Challis, Katie</author><author>Macherla,

Chitralekha</author><author>Nevalainen, Erica</author><author>Degitz, Sigmund J.</author></authors></contributors><titles><title>In Vitro, Ex Vivo, and In Vivo Determination of Thyroid Hormone Modulating Activity of Benzothiazoles</title><secondary-title>Toxicological Sciences</secondary-title></titles><periodical><full-title>Toxicological Sciences</full-title></periodical><pages>254-264</pages><volume>146</volume><number>2</number><dates><year>2015</year></dates><isbn>1096-6080</isbn><urls><related-urls><url>http://dx.doi.org/10.1093/toxsci/kfv090</url></related-urls></urls><electronic-resource-num>10.1093/toxsci/kfv090</electronic-resource-num></record></Cite></EndNote>].

The development and implementation of this approach to identify potential NIS inhibitors fills a critical gap in the capability to screen chemicals under the U.S.EPA's regulatory purview for thyroid disrupting activity. The findings reported here confirm that the cell-based screening approach can be effectively used to identify chemicals that directly compete with iodide for intracellular transport through the symporter, as well as those chemicals that alter NIS function by disruption of energy production required to maintain the sodium gradient. The use of a unique ranking system that incorporates the cytotoxicity response for each chemical provides a stronger foundation for further assessment of chemicals with commonalities in structural and toxicological properties and/or prioritization for further testing. Because of the likely alternative RAIU inhibition mechanisms among these chemicals, close examination of the dose-response is suggested rather than relying on a single metric such as the AC_{50} or $absEC_{50}$ to draw conclusions regarding NIS inhibition. In addition, as with most *in vitro* assays, chemical purity and solubility

limitations need to be considered, warranting additional secondary assay testing to further confirm initial findings for high priority chemicals. For example, a secondary assay such as the rat thyroid FRTL-5 cell line based RAIU assay would add confidence to any HTS findings. Lastly, as with any *in vitro* assay, considerations of absorption, distribution, metabolism, excretion (ADME) as well as potential compensatory feedback are needed before assuming that a chemical would result in altered thyroid synthesis with exposure *in vivo*. Additional studies using short-term *in vivo* assays, such as those that employ amphibian or weanling rat models, are warranted to further investigate the thyroid-disruptive potential of NIS inhibitors.

As public concern increases over the effects of environmental chemicals on thyroid hormone signaling, there is an urgent need to expand the current knowledge base and understanding of the risks of thyroid disruption by a broader range of compounds. Iodide uptake into the thyroid via NIS is the critical initial step of thyroid hormone biosynthesis and is a known target of thyroid disruption in humans and wildlife. The screening of 293 ToxCast chemicals in the current study represents the first large scale effort to investigate NIS as a molecular target of environmental chemicals that cover a broad spectrum of structural and toxicological properties. The ranking of potential NIS inhibitors can inform the prioritization of chemicals for secondary testing. This ranking method will prove useful for the imminent screening of the ToxCast phase II and e1K chemical libraries for putative NIS inhibitors. Moreover, these data provide an integral component of the U.S.EPA's EDSP initiative to expand the coverage of known molecular targets of chemical-induced thyroid disruption (Noyes *et al.* 2017), as well as to support the development of a series of OECD test guidelines to assess chemicals for thyroid disrupting activity.

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Supplemental Data Description

Supplemental Figure 1: Assay plate map.

Supplemental Figure 2: Dose-response curves of all chemicals tested in multi-concentration

Supplemental Figure 3: Does-response curves of sodium perchlorate and DCNQ positive controls in multi-concentration screening

Supplemental Table 1: AC50s of the 10 internally replicated chemicals tested in multi-concentration

Supplemental Table 2: Chemical Potency Metrics Summary Table

Supplemental File 1: Documented Data Analysis in R

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Reference

[ADDIN EN.REFLIST]

Abbreviations

EDSP21 (Endocrine Disruptor Screening Program in the 21st century), OECD (The Organization for Economic Co-operation and Development), ToxCast (Toxicity Forecaster), CV (coefficient of variation), NIS (sodium iodide symporter), RAIU (radioactive iodide uptake), RLU (relative light unit), SD (standard deviation), T_3 (triiodothyronine), T_4 (thyroxine), TH (thyroid hormone), 3bMAD (three times the baseline median absolute deviation), DMSO (dimethylsulfoxide), 2,4-D (2,4-dichlorophenoxyacetic acid), DCNQ (2,3-dichloro-1,4-napthoquinone), HEK (human embryonic kidney), AOP (adverse outcome pathway), HTS (high-throughput screening), DMEM (Dulbecco's Modified Eagle Medium), CPM (counts per minute), TAA (toxicity-adjusted area), PFOS (perfluorooctanesulfonic acid), PFOA (perfluorooctanoic acid)

Figures

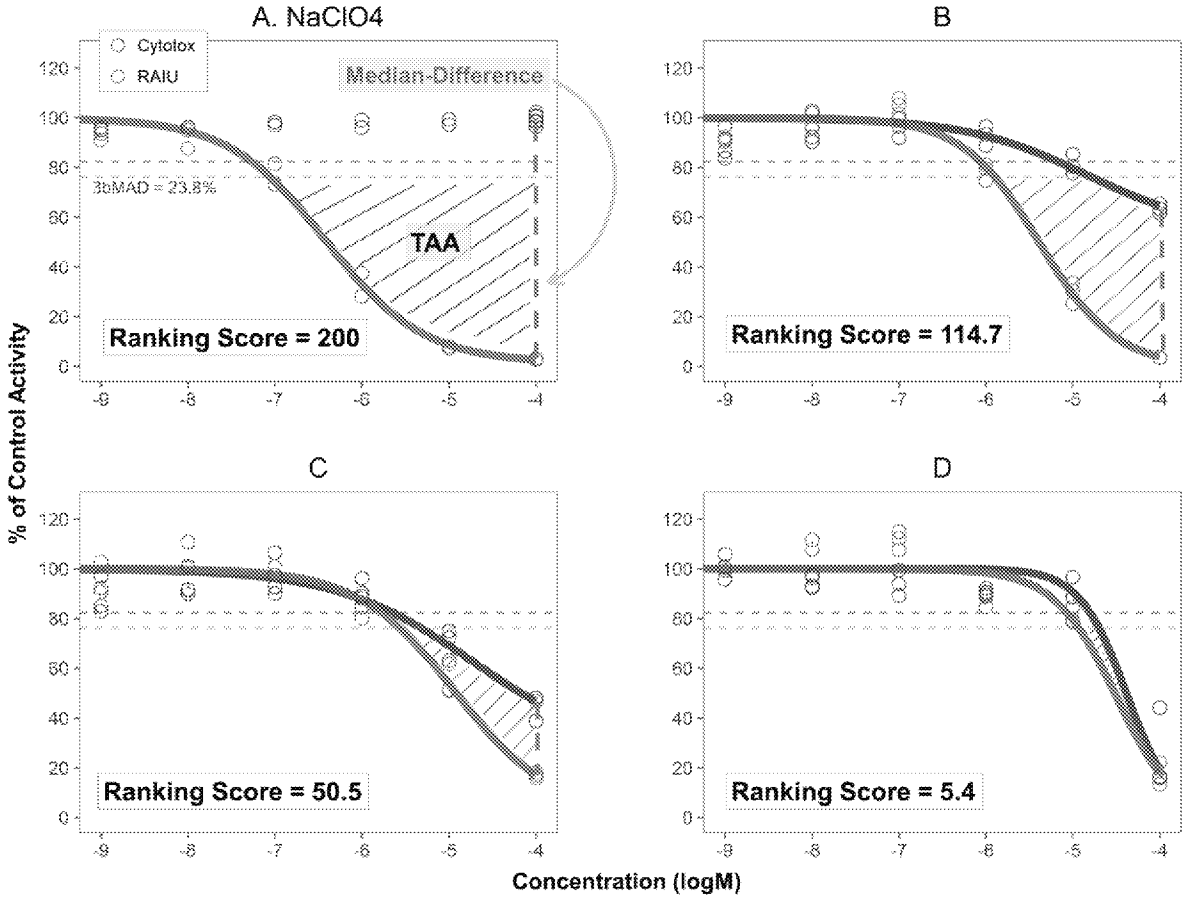


Fig. 1. Demonstration of ranking score, TAA and Median-Difference. Examples of chemical responses: A) sodium perchlorate, B) triphenyltin hydroxide, C) folpet, D) prodiamine. Cell viability and RAIU assay results are illustrated in red and blue respectively. The red and blue horizontal dotted lines represent the 3bMAD threshold for cell viability and RAIU assay respectively. Toxicity-adjusted area (TAA) is the gray striped area defined by 1) maximum concentration vertical line (right border), 2) the 3bMAD significant threshold horizontal line for RAIU assay (top border; blue dashed line), 3) the dose-response curve of RAIU and 4) if present,

the dose-response curve of cytotoxicity. The difference of median responses of RAIU and cytotoxicity at maximum tested concentration (Median-Difference) is indicated by the green vertical dotted line. Sodium perchlorate (A) was chosen as the reference NIS inhibitor to normalize test chemical TAA and Median-Difference as percentage values. Ranking score is obtained as the sum of normalized TAA and Median-Difference values. Therefore, sodium perchlorate has a ranking score of 200. B, C and D show three test chemicals with less RAIU inhibition and more cytotoxicity relative to sodium perchlorate. As the TAA and Median-Difference values decrease, their ranking scores also decrease.

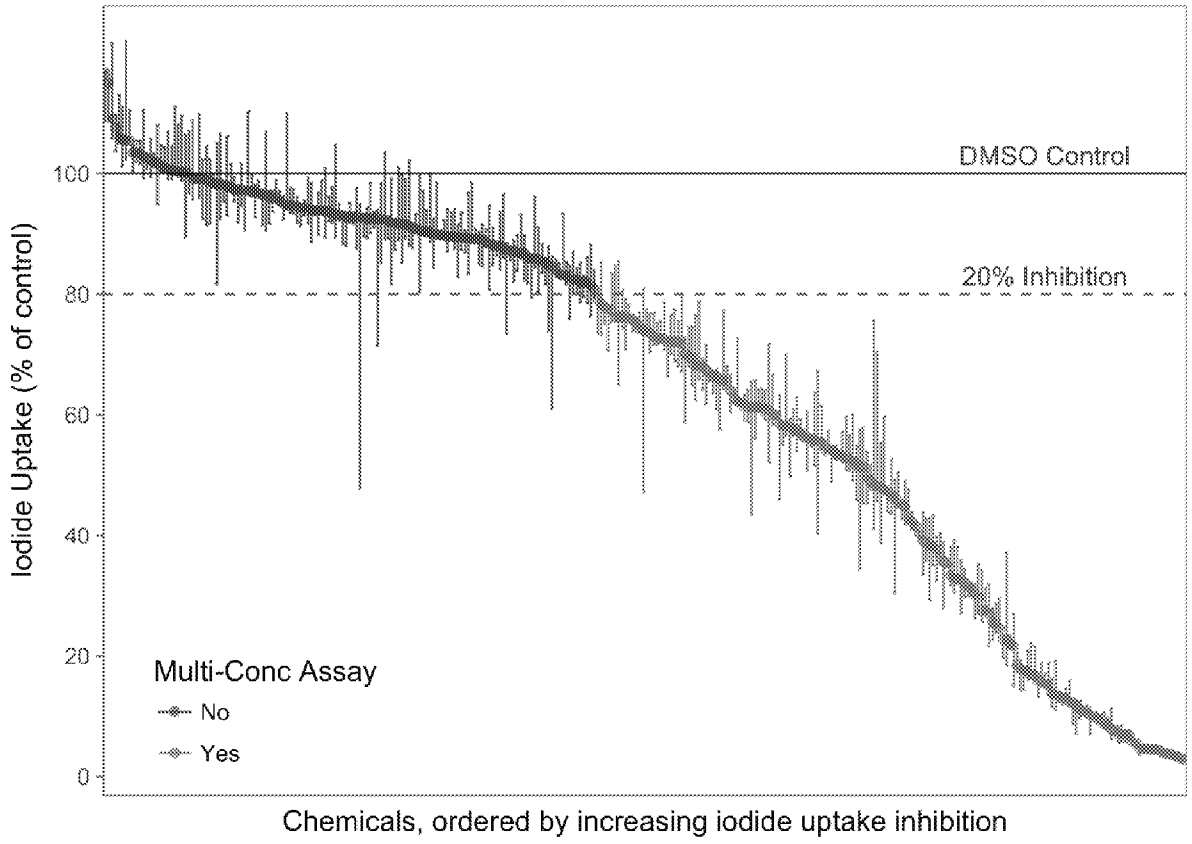


Fig. 2. Median and range of test chemical responses in single-concentration RAIU screening. Median response of each chemical is represented by the dot and vertical bar shows the maximal iodide uptake (top of the bar) and the minimum iodide uptake (bottom of the bar). The pink horizontal line represents the 20% inhibition threshold. 310 blinded samples were tested at maximum permissible concentrations (typically 100 μM). 169 chemicals (54.5%) were selected for multi-concentration testing based on a 20% inhibition activity threshold.

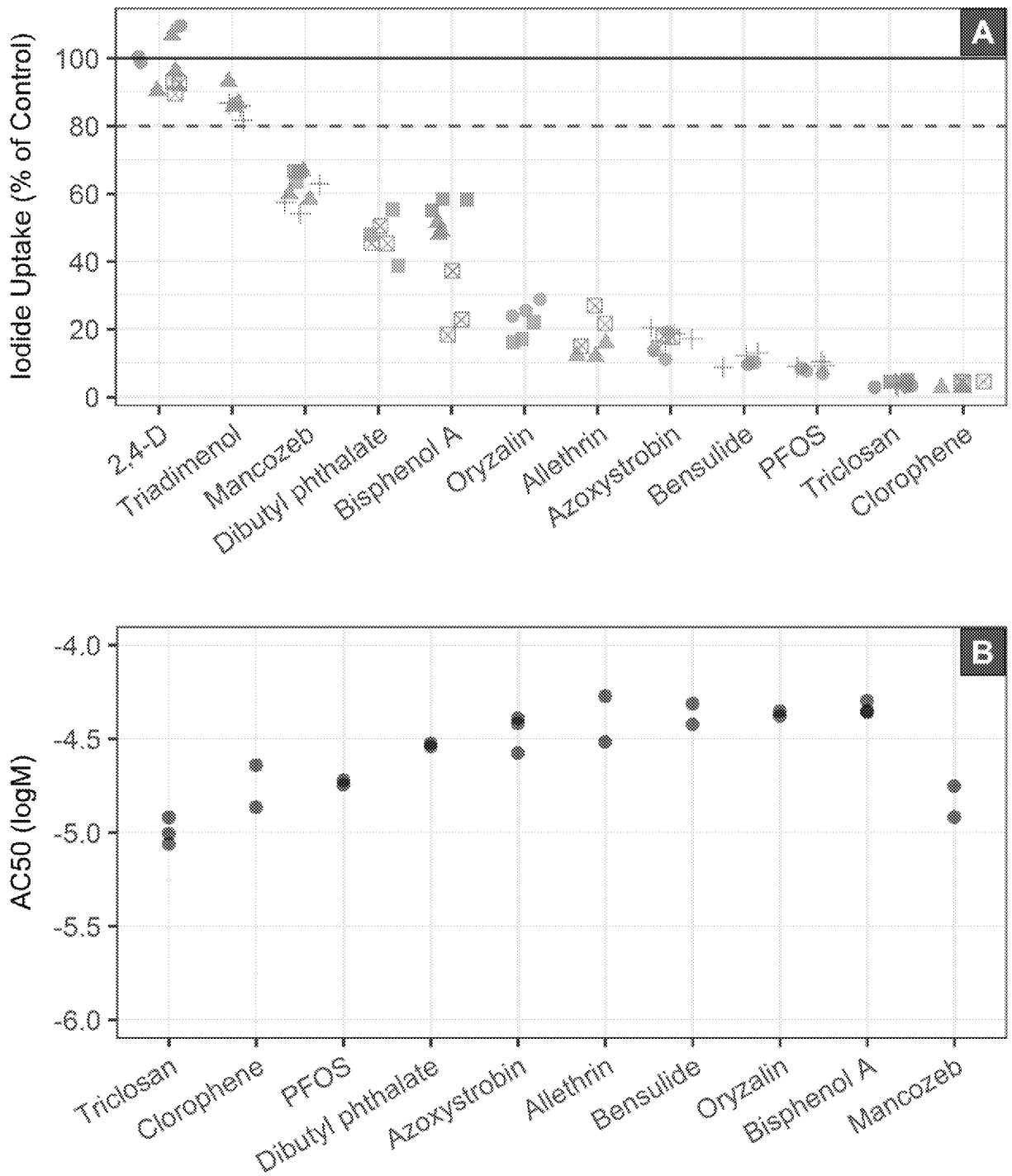

A
Iodide Uptake (% of Control)
100
80
60
40
20
0
2,4-D
Triadimenol
Mancozeb
Dibutyl phthalate
Bisphenol A
Oryzalin
Allethrin
Azoxystrobin
Bensulide
PFOS
Triclosan
Clorophene
B
AC50 (logM)
-4.0
-4.5
-5.0
-5.5
-6.0
Triclosan
Clorophene
PFOS
Dibutyl phthalate
Azoxystrobin
Allethrin
Bensulide
Oryzalin
Bisphenol A
Mancozeb

Fig. 3. (A) Responses of internal replicates in single-concentration screening. 12 chemicals in the ToxCast phase1_v2 library were replicated 2 or 3 times (supplied in 2 or 3 blinded chemical samples). Colors represent different chemicals, while shapes indicate different internally replicated samples for a given chemical. Since each sample was tested in three bioreplicates, each shape for a given chemical has three data points. Ten of the 12 replicated chemicals that gave >20% inhibition (pink horizontal line) in this single-concentration test were subsequently tested in multi-concentration format (Fig. 3B). **(B) AC_{50} of internal replicates in multi-concentration screening.** Each symbol represents one AC50 value obtained from one sample of the chemical tested in three bioreplicates in multi-concentration.

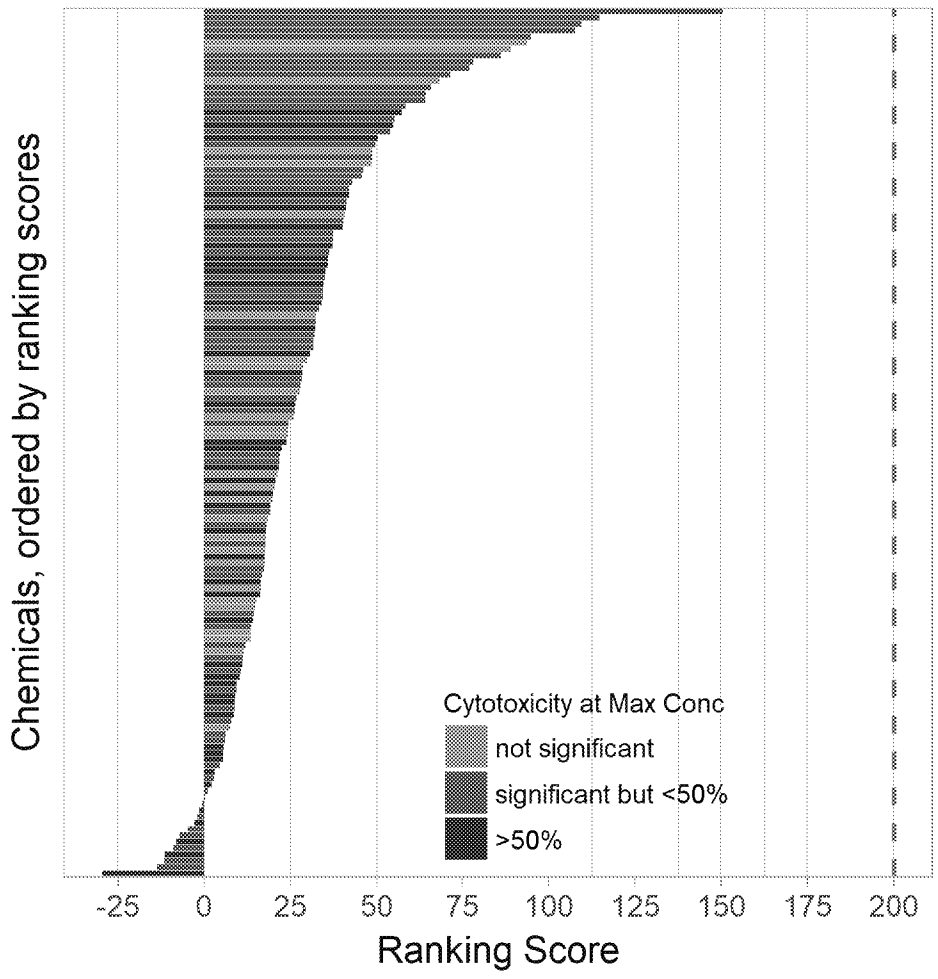


Fig. 4. Ranking scores for chemical samples tested in multi-concentration screening. Ranking scores were evaluated only if a chemical produced significant RAIU inhibition. Of the 169 chemical samples tested in multi-concentration, 32 did not show significant RAIU inhibition and were therefore excluded from the ranking analysis. The vertical dotted line is the ranking score of sodium perchlorate, which was used as the reference chemical in the ranking analysis. The ranking score of the 137 test chemical samples ranged from 150.41 to -29.52, with 4 having ranking score >100, 17 having ranking score between 50 and 100, and 116 having ranking score <50.

Cytotoxicity levels at the maximum testing concentration are indicated in colors shown. Of the 137 chemical samples that produced significant RAIU inhibition, 27 exhibited no cytotoxicity, 67 exhibited significant but <50% cytotoxicity, and 43 exhibited >50% cytotoxicity at the maximum concentration tested.

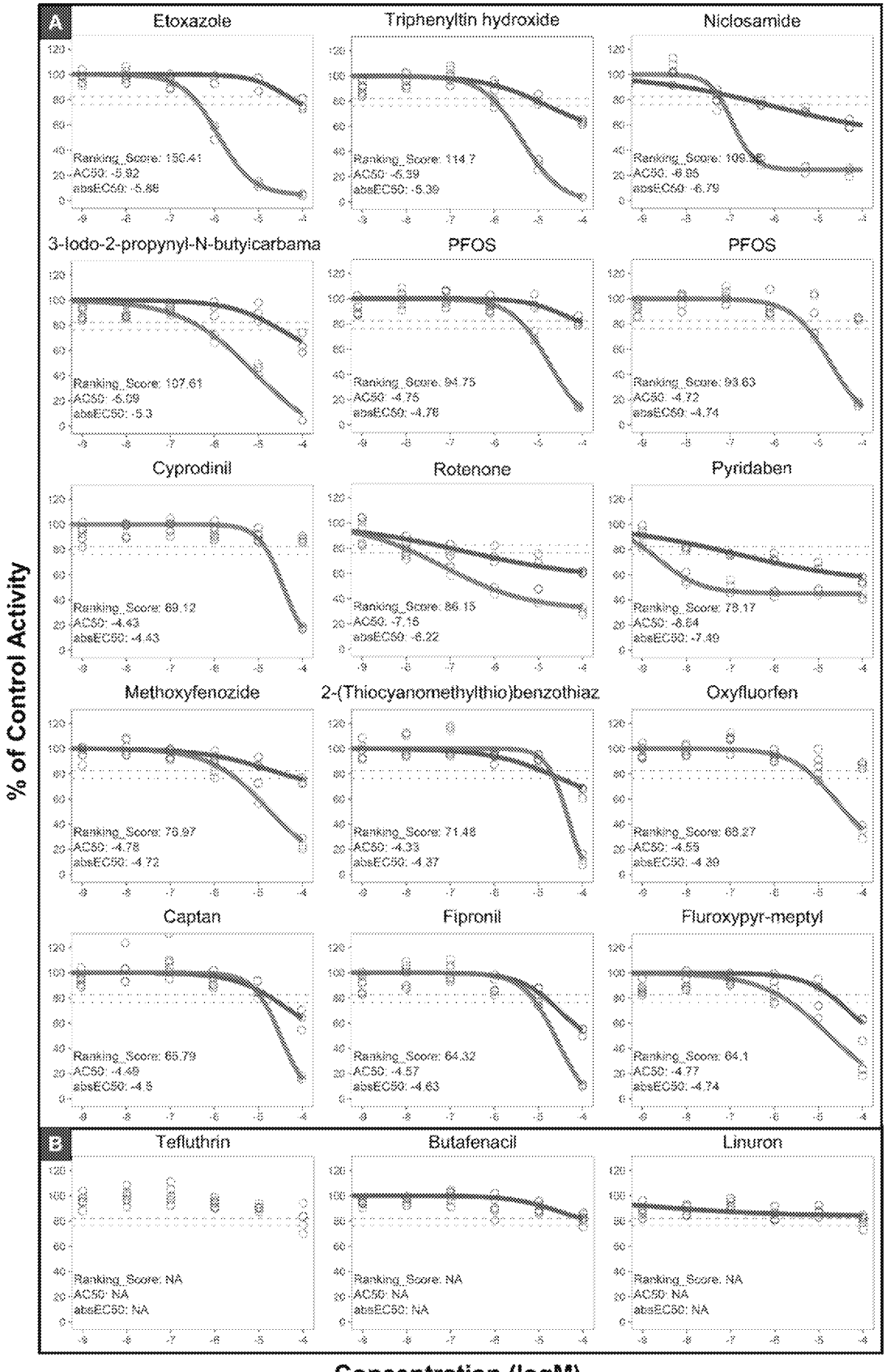

A
Etoxazole
Ranking_Score: 150.41
AC50: -5.92
absEC50: -5.86
Triphenyltin hydroxide
Ranking_Score: 114.7
AC50: -5.39
absEC50: -5.39
Niclosamide
Ranking_Score: 109.86
AC50: -6.85
absEC50: -6.79
3-Iodo-2-propynyl-N-butylcarbama
Ranking_Score: 107.61
AC50: -5.09
absEC50: -5.3
PFOS
Ranking_Score: 94.75
AC50: -4.75
absEC50: -4.76
PFOS
Ranking_Score: 93.63
AC50: -4.72
absEC50: -4.74
Cyprodinil
Ranking_Score: 89.12
AC50: -4.43
absEC50: -4.43
Rotenone
Ranking_Score: 86.15
AC50: -7.15
absEC50: -6.22
Pyridaben
Ranking_Score: 79.17
AC50: -6.84
absEC50: -7.49
Methoxyfenozide
Ranking_Score: 79.97
AC50: -4.78
absEC50: -4.72
2-(Thiocyanomethylthio)benzothiaz
Ranking_Score: 71.48
AC50: -4.33
absEC50: -4.37
Oxyfluorfen
Ranking_Score: 68.27
AC50: -4.55
absEC50: -4.39
Captan
Ranking_Score: 65.79
AC50: -4.49
absEC50: -4.5
Fipronil
Ranking_Score: 64.32
AC50: -4.57
absEC50: -4.63
Fluroxypyr-meptyl
Ranking_Score: 64.1
AC50: -4.77
absEC50: -4.74
B
Tefluthrin
Ranking_Score: NA
AC50: NA
absEC50: NA
Butafenacil
Ranking_Score: NA
AC50: NA
absEC50: NA
Linuron
Ranking_Score: NA
AC50: NA
absEC50: NA
% of Control Activity
Concentration (logM)

Fig. 5. Dose response, ranking score, AC50 and absEC50 of (A) top 15 ranked samples (14 chemicals) and (B) example chemicals that did not produce significant RAIU inhibition. Chemical responses (for three bioreplicates) are shown as circles with red representing cytotoxicity assay results and blue representing RAIU assay results. The red and blue horizontal dotted lines represent the 3bMAD threshold for cell viability and RAIU assay, respectively. AC_{50} and $absEC_{50}$ are expressed as logM.

Tables

Table 1. Control chemicals included on each assay plate

Control Chemical	DMSO	2,4-D	DCNQ	NaClO4	$NaNO_3$	NaSCN
CAS No.	67-68-5	94-75-7	117-80-6	7601-89-0	7631-99-4	540-72-7
Purity (%)	99.9	98	98	98	99	98
Purpose	Vehicle control	Negative control	Cell viability assay, positive control	RAIU assay, positive control	RAIU assay, positive control (20% inhibition)	RAIU assay, positive control (80% inhibition)
Concentration (% or M)	0.5%	1E-4	1E-9, 1E-8, 1E-7, 1E-6, 1E-5, 1E-4	1E-9, 1E-8, 1E-7, 1E-6, 1E-5, 1E-4	1E-4	1E-4
Reps*/plate in Single-Con Screening	12	2	3 for 1E-4M, 1 for the rest	6 for 1E-4M, 2 for the rest	2	2
Reps*/plate in Multi-Con Screening	8	2	3 for 1E-4M, 1 for the rest	6 for 1E-4M, 2 for the rest	2	2

*Number of wells

Table 2. List of test chemicals and screening results

Max Conc: the maximum permissible concentration tested in single-concentration screening. Serial dilution of samples for multi-concentration assay started with this concentration.

*: precipitate visually observed in the well of stock chemical plate.

Hit call: indicates whether chemical median RAIU inhibition was over 20% in single-concentration screening. +: yes, -: no.

AC_{50}: the AC_{50} value derived from multi-concentration dose-response curve.

$absEC_{50}$: the $absEC_{50}$ value derived from multi-concentration dose-response curve if the maximum inhibition achieved by the chemical was over 50%.

Cytotox-point: the log concentration where the chemical started to show significant toxicity ($absEC_{82.3}$).

	Chemical	CAS NO.	Max Conc(M)	Hit Call	AC50	absEC50	Cytotox Point	Ranking Score
1	Etoxazole	153233-91-1	1.00E-04	+	-5.92	-5.88	-4.32	150.41
2	Triphenyltin hydroxide	76-87-9	1.00E-04	+	-5.39	-5.39	-5.17	114.70
3	Niclosamide	50-65-7	5.00E-05	+	-6.95	-6.79	-6.91	109.38
4	3-Iodo-2-propynyl-N-butylcarbamate	55406-53-6	1.00E-04	+	-5.09	-5.30	-4.80	107.61
5	PFOS	1763-23-1	8.00E-05	+	-4.75	-4.78	-4.09	94.75
6	PFOS	1763-23-1	8.00E-05	+	-4.72	-4.74	NA	93.63
7	Cyprodinil	121552-61-2	1.00E-04	+	-4.43	-4.43	NA	89.12
8	Rotenone	83-79-4	1.00E-04	+	-7.15	-6.22	-7.30	86.15
9	Pyridaben	96489-71-3	1.00E-04	+	-8.64	-7.49	-7.60	78.17
10	Methoxyfenozide	161050-58-4	1.00E-04	+	-4.78	-4.72	-4.68	76.97
11	2-(Thiocyanomethylthio)benzothiazole	21564-17-0	1.00E-04	+	-4.33	-4.37	-4.91	71.48
12	Oxyfluorfen	42874-03-3	1.00E-04	+	-4.55	-4.39	NA	68.27
13	Captan	133-06-2	9.50E-05	+	-4.49	-4.50	-4.81	65.79
14	Fipronil	120068-37-3	1.00E-04	+	-4.57	-4.63	-4.92	64.32
15	Fluroxypyr-meptyl	81406-37-3	1.00E-04	+	-4.77	-4.74	-4.74	64.10
16	Cyhalofop-butyl	122008-85-9	9.50E-05	+	-5.47	-4.75	-5.07	58.47
17	Fenpyroximate (Z,E)	111812-58-9	1.00E-04	+	-6.79	-6.07	-7.09	57.34
18	Thiobencarb	28249-77-6	1.00E-04	+	-4.38	-4.34	-4.70	55.20
19	Emamectin benzoate	155569-91-8	1.00E-04	+	-4.88	-4.99	-5.18	54.82
20	Diphenylamine	122-39-4	1.00E-04	+	-4.74	-4.28	-5.59	54.01
21	Folpet	133-07-3	1.00E-04	+	-4.93	-4.92	-5.65	50.48
22	Endosulfan	115-29-7	1.00E-04	+	-4.35	-4.39	-4.92	49.72
23	Prometryn	7287-19-6	1.00E-04	+	-4.44	NA	NA	48.73
24	Zoxamide	156052-68-5	1.00E-04	+	-4.48	-4.37	-4.66	48.72
25	Cyazofamid	120116-88-3	1.00E-04	+	-5.59	NA	NA	48.49
26	Parathion	56-38-2	1.00E-04	+	-4.72	-4.49	-4.01	46.24
27	Fenthion	55-38-9	1.00E-04	+	-4.40	-4.18	-3.72	45.87
28	Mancozeb	8018-01-7	5.00E-05	+	-4.92	NA	-4.80	43.00
29	Bifenazate	149877-41-8	1.00E-04	+	-4.42	-4.39	-4.87	42.05

30	Clorophene	120-32-1	1.00E-04	+	-4.87	-5.07	-4.68	41.98
31	Trifloxystrobin	141517-21-7	1.00E-04	+	-5.67	-5.05	-5.99	41.32
32	Triclosan	3380-34-5	1.00E-04	+	-5.01	-5.00	-4.98	41.22
33	Methoxychlor	72-43-5	9.50E-05	+	-4.58	NA	NA	40.75
34	Quinoxyfen	124495-18-7	1.00E-04	+	-4.47	-4.44	-4.85	40.43
35	Triflumizole	68694-11-1	1.00E-04	+	-4.53	-4.61	-4.82	40.28
36	Prallethrin	23031-36-9	9.50E-05	+	-4.38	-4.33	-4.66	37.48
37	S-Bioallethrin	28434-00-6	1.00E-04	+	-4.42	-4.37	-4.62	37.39
38	Coumaphos	56-72-4	1.00E-04	+	-5.00	-4.79	-4.95	37.24
39	Chlorpyrifos-methyl	5598-13-0	1.00E-04	+	-5.01	NA	-5.16	36.26
40	Fluoxastrobin	361377-29-9	1.00E-04	+	-4.95	-4.84	-5.63	35.85
41	Triclosan	3380-34-5	1.00E-04	+	-5.06	-5.11	-5.13	35.85
42	Pyraclostrobin	175013-18-0	1.00E-04	+	-6.02	-5.91	-6.27	35.19
43	Fenoxaprop-ethyl	66441-23-4	1.00E-04	+	-4.53	-4.09	-5.05	35.03
44	Fenoxycarb	72490-01-8	1.00E-04	+	-4.47	-4.51	-4.91	34.58
45	Hexaconazole	79983-71-4	1.00E-04	+	-4.45	-4.13	-4.55	34.50
46	Diclosulam	145701-21-9	1.00E-04	+	-4.82	NA	-4.92	34.38
47	Clorophene	120-32-1	1.00E-04	+	-4.64	-4.75	-4.69	34.14
48	Tebupirimfos	96182-53-5	1.00E-04	+	-4.61	-4.42	-4.54	33.31
49	Abamectin	71751-41-2	1.00E-04*	+	-4.33	NA	NA	32.50
50	Pyriproxyfen	95737-68-1	1.00E-04	+	-4.70	-4.11	-4.90	32.40
51	Triclosan	3380-34-5	1.00E-04	+	-4.92	-4.90	-5.01	32.32
52	Carfentrazone-ethyl	128639-02-1	1.00E-04	+	-4.35	-4.03	-4.40	31.97
53	Pirimiphos-methyl	29232-93-7	1.00E-04	+	-4.43	NA	-4.18	31.71
54	Dibutyl phthalate	84-74-2	1.00E-04	+	-4.54	NA	-3.98	31.65
55	Methylene bis(thiocyanate)	6317-18-6	1.00E-04	+	-4.66	-4.79	-4.86	30.68
56	Bisphenol A	80-05-7	1.00E-04	+	-4.36	NA	NA	29.86
57	Dithiopyr	97886-45-8	9.50E-05	+	-4.65	NA	NA	28.75
58	Tebufenpyrad	119168-77-3	1.00E-04	+	-5.60	-5.82	-6.21	28.57
59	Diclofop-methyl	51338-27-3	1.00E-04	+	-4.49	-4.12	-4.51	28.35
60	Dibutyl phthalate	84-74-2	1.00E-04	+	-4.53	NA	-4.29	28.05
61	Lactofen	77501-63-4	1.00E-04	+	-4.79	NA	NA	27.70
62	Piperonyl butoxide	51-03-6	1.00E-04	+	-4.22	NA	-4.87	26.83
63	Buprofezin	69327-76-0	1.00E-04	+	-4.55	-4.61	-4.95	26.43
64	Cloprop	101-10-0	1.00E-04	+	-4.49	NA	-3.45	26.25
65	Flutolanil	66332-96-5	1.00E-04	+	-4.50	NA	NA	25.91
66	Cinmethylin	87818-31-3	1.00E-04	+	-4.23	NA	-4.43	24.38
67	Chlorpropham	101-21-3	1.00E-04	+	-4.42	NA	NA	24.33
68	Clodinafop-propargyl	105512-06-9	1.00E-04	+	-5.70	NA	NA	24.25
69	Phosalone	2310-17-0	1.00E-04	+	-4.46	-4.35	-4.59	23.91
70	Allethrin	584-79-2	1.00E-04	+	-4.52	-4.49	-4.82	22.64
71	Disulfoton	298-04-4	1.00E-04	+	-4.27	NA	-4.44	21.93
72	Flumiclorac-pentyl	87546-18-7	1.00E-04	+	-4.50	-4.16	-5.26	21.87
73	Forchlorfenuron	68157-60-8	1.00E-04	+	-4.44	-4.50	-4.94	21.64
74	Flumetralin	62924-70-3	1.00E-04	+	-4.33	NA	NA	21.33
75	Ethalfluralin	55283-68-6	1.00E-04	+	-5.16	-4.93	-5.93	20.66
76	Lindane	58-89-9	1.00E-04	+	-4.32	NA	NA	20.50
77	Fluazinam	79622-59-6	9.00E-05	+	-5.16	-5.13	-5.40	20.06
78	Cyfluthrin	68359-37-5	1.00E-04	+	-4.57	NA	NA	19.87
79	Tri-allate	2303-17-5	1.00E-04	+	-4.61	-4.57	-4.84	19.20
80	Imazalil	35554-44-0	1.00E-04	+	-4.50	NA	-4.94	19.16
81	Cypermethrin	52315-07-8	1.00E-04	+	-4.96	NA	NA	18.48
82	Amitraz	33089-61-1	1.00E-04	+	-4.22	NA	-4.94	18.15
83	Tetraconazole	112281-77-3	9.50E-05	+	-4.65	-4.33	-4.86	18.01
84	Thiazopyr	117718-60-2	1.00E-04	+	-4.62	NA	NA	17.88
85	Trifluralin	1582-09-8	1.00E-04	+	-4.95	NA	-5.61	17.76
86	Tebufenozide	112410-23-8	1.00E-04	+	-4.68	NA	NA	17.75

87	Azoxystrobin	131860-33-8	1.00E-04	+	-4.58	-4.59	-5.04	17.64
88	Mancozeb	8018-01-7	5.00E-05	+	-4.75	NA	NA	17.52
89	Fluazifop-butyl	69806-50-4	1.00E-04	+	-4.36	NA	-4.26	17.41
90	Fenarimol	60168-88-9	1.00E-04	+	-5.11	NA	-1.70	16.84
91	Allethrin	584-79-2	1.00E-04	+	-4.27	-4.24	-4.69	16.46
92	Maneb	12427-38-2	1.00E-04	+	-4.37	NA	NA	16.39
93	Flusilazole	85509-19-9	1.00E-04	+	-4.25	-4.16	-4.66	16.20
94	Bisphenol A	80-05-7	1.00E-04	+	-4.35	NA	NA	15.20
95	Ametryn	834-12-8	1.00E-04	+	-4.26	NA	NA	14.78
96	Fluazifop-P-butyl	79241-46-6	1.00E-04	+	-4.41	NA	-4.84	14.47
97	Diniconazole	83657-24-3	1.00E-04	+	-4.50	-4.56	-4.79	14.21
98	Pendimethalin	40487-42-1	1.00E-04	+	-4.32	NA	-4.36	13.68
99	Fenitrothion	122-14-5	1.00E-04	+	-4.49	NA	NA	13.48
100	Isazofos	42509-80-8	1.00E-04	+	-4.26	NA	NA	13.45
101	Oxadiazon	19666-30-9	1.00E-04	+	-4.30	NA	-4.43	12.04
102	Hexythiazox	78587-05-0	1.00E-04	+	-4.46	NA	NA	11.36
103	Fenamidone	161326-34-7	1.00E-04	+	-4.29	NA	-4.09	11.25
104	Difenoconazole	119446-68-3	1.00E-04	+	-4.75	-4.90	-5.09	11.04
105	Fluthiacet-methyl	117337-19-6	1.00E-04	+	-4.72	NA	-3.59	10.68
106	Azoxystrobin	131860-33-8	1.00E-04	+	-4.42	-4.47	-5.06	10.24
107	Oryzalin	19044-88-3	1.00E-04	+	-4.38	-4.17	-4.63	9.45
108	Thidiazuron	51707-55-2	1.00E-04	+	-4.44	NA	-4.23	9.43
109	Famoxadone	131807-57-3	1.00E-04	+	-5.69	-4.81	-6.04	8.99
110	Dicofol	115-32-2	1.00E-04	+	-4.54	-4.61	-4.72	8.89
111	Propargite	2312-35-8	1.00E-04	+	-4.40	NA	-4.64	8.80
112	2,2-Bis(4-hydroxyphenyl)-1,1,1-trichloroethane	2971-36-0	1.00E-04	+	-4.39	-4.46	-4.90	8.69
113	Propiconazole	60207-90-1	1.00E-04	+	-4.39	NA	-4.75	7.91
114	Chlorethoxyfos	54593-83-8	1.00E-04	+	-4.41	NA	NA	7.53
115	Thiodicarb	59669-26-0	1.00E-04	+	-4.91	NA	-4.83	6.17
116	Ethofumesate	26225-79-6	1.00E-04	+	-4.52	NA	-4.56	6.01
117	Bensulide	741-58-2	1.00E-04	+	-4.42	-4.43	-4.83	5.59
118	Prodiamine	29091-21-2	1.00E-04	+	-4.49	-4.52	-4.80	5.44
119	Bensulide	741-58-2	1.00E-04	+	-4.31	-4.34	-4.72	5.44
120	Bisphenol A	80-05-7	1.00E-04	+	-4.30	NA	-3.77	4.51
121	Flumioxazin	103361-09-7	1.00E-04	+	-4.38	-4.40	-4.84	3.04
122	Methidathion	950-37-8	1.00E-04	+	-4.42	NA	-4.22	2.81
123	Azoxystrobin	131860-33-8	1.00E-04	+	-4.39	-4.39	-5.02	2.15
124	Butralin	33629-47-9	1.00E-04	+	-4.35	NA	-4.67	1.05
125	Dicloran	99-30-9	1.00E-04	+	-4.63	NA	-5.03	0.28
126	Oryzalin	19044-88-3	1.00E-04	+	-4.35	NA	-4.60	-0.65
127	Fenbuconazole	114369-43-6	1.00E-04	+	-4.27	-4.30	-4.72	-1.43
128	Thiram	137-26-8	1.00E-04	+	-4.18	-4.04	-4.88	-2.03
129	Tetramethrin	7696-12-0	1.00E-04	+	-4.41	-4.32	-4.88	-2.91
130	Profenofos	41198-08-7	5.00E-05	+	-4.55	NA	-4.90	-4.66
131	Quizalofop-ethyl	76578-14-8	8.50E-05	+	-4.42	NA	-4.65	-7.22
132	Prochloraz	67747-09-5	1.00E-04	+	-4.18	-4.12	-4.69	-8.05
133	Milbemectin (mixture of 70% Milbemcin A4, 30% Milbemycin A3)	NOCAS_34742	9.50E-05	+	-4.22	NA	-5.04	-8.94
134	Captafol	2425-06-1	1.00E-04	+	-4.45	-4.49	-5.06	-11.37
135	Tribufos	78-48-8	1.00E-04	+	-4.94	NA	-5.22	-11.50
136	Benfluralin	1861-40-1	1.00E-04	+	-4.62	NA	-4.78	-13.71
137	MGK-264	113-48-4	1.00E-04	+	-4.28	NA	-4.73	-29.52
138	Chlorothalonil	1897-45-6	1.00E-04	+	NA	NA	-4.03	NA
139	Propanil	709-98-8	1.00E-04	+	NA	NA	-3.88	NA
140	Bromoxynil	1689-84-5	8.00E-05	+	NA	NA	-5.22	NA

141	Napropamide	15299-99-7	1.00E-04	+	NA	NA	NA	NA
142	Nitrapyrin	1929-82-4	1.00E-04	+	NA	NA	NA	NA
143	Propetamphos	31218-83-4	1.00E-04	+	NA	NA	NA	NA
144	Myclobutanil	88671-89-0	1.00E-04	+	NA	NA	NA	NA
145	Malathion	121-75-5	1.00E-04	+	NA	NA	-4.32	NA
146	Resmethrin	10453-86-8	1.00E-04	+	NA	NA	-4.41	NA
147	Fenpropathrin	39515-41-8	1.00E-04	+	NA	NA	NA	NA
148	Picloram	1918-02-1	1.00E-04	+	NA	NA	NA	NA
149	Fludioxonil	131341-86-1	1.00E-04	+	NA	NA	-4.17	NA
150	Acibenzolar-S-methyl	135158-54-2	1.00E-04	+	NA	NA	NA	NA
151	Azinphos-methyl	86-50-0	1.00E-04	+	NA	NA	-3.99	NA
152	Mancozeb	8018-01-7	5.00E-05	+	NA	NA	NA	NA
153	Boscalid	188425-85-6	1.00E-04	+	NA	NA	-3.30	NA
154	Butachlor	23184-66-9	1.00E-04	+	NA	NA	-4.37	NA
155	Tefluthrin	79538-32-2	1.00E-04	+	NA	NA	NA	NA
156	Butafenacil	134605-64-4	1.00E-04	+	NA	NA	-4.04	NA
157	Tralkoxydim	87820-88-0	1.00E-04	+	NA	NA	NA	NA
158	Pyraflufen-ethyl	129630-19-9	1.00E-04	+	NA	NA	-4.33	NA
159	Prometon	1610-18-0	1.00E-04	+	NA	NA	NA	NA
160	Vinclozolin	50471-44-8	1.00E-04	+	NA	NA	NA	NA
161	2-Phenylphenol	90-43-7	1.00E-04	+	NA	NA	NA	NA
162	Clomazone	81777-89-1	1.00E-04	+	NA	NA	NA	NA
163	Flufenpyr-ethyl	188489-07-8	1.00E-04	+	NA	NA	NA	NA
164	Chlorpyrifos oxon	5598-15-2	9.50E-05	+	NA	NA	-4.01	NA
165	Fenhexamid	126833-17-8	1.00E-04	+	NA	NA	-4.15	NA
166	Cycloate	1134-23-2	1.00E-04	+	NA	NA	NA	NA
167	Naled	300-76-5	1.00E-04	+	NA	NA	NA	NA
168	Linuron	330-55-2	1.00E-04	+	NA	NA	NA	NA
169	EPTC	759-94-4	1.00E-04	+	NA	NA	NA	NA
170	Bifenthrin	82657-04-3	1.00E-04	-	NA	NA	NA	NA
171	Bentazone	25057-89-0	1.00E-04	-	NA	NA	NA	NA
172	Mesotrione	104206-82-8	1.00E-04	-	NA	NA	NA	NA
173	Esfenvalerate	66230-04-4	1.00E-04	-	NA	NA	NA	NA
174	Thiophanate-methyl	23564-05-8	1.00E-04	-	NA	NA	NA	NA
175	Trichlorfon	52-68-6	1.00E-04	-	NA	NA	NA	NA
176	Carbaryl	63-25-2	1.00E-04	-	NA	NA	NA	NA
177	2,4-Dichlorophenoxyacetic acid	94-75-7	1.00E-04	-	NA	NA	NA	NA
178	Boric acid	10043-35-3	1.00E-04	-	NA	NA	NA	NA
179	Dichlorprop	120-36-5	1.00E-04	-	NA	NA	NA	NA
180	Dicrotophos	141-66-2	1.00E-04	-	NA	NA	NA	NA
181	Butylate	2008-41-5	1.00E-04	-	NA	NA	NA	NA
182	Dimethylarsinic acid	75-60-5	1.00E-04	-	NA	NA	NA	NA
183	Dichlorvos	62-73-7	5.00E-05	-	NA	NA	NA	NA
184	Malaoxon	1634-78-2	1.00E-04	-	NA	NA	NA	NA
185	Cyanazine	21725-46-2	1.00E-04	-	NA	NA	NA	NA
186	Methomyl	16752-77-5	1.00E-04	-	NA	NA	NA	NA
187	PFOA	335-67-1	1.00E-04	-	NA	NA	NA	NA
188	Propoxur	114-26-1	1.00E-04	-	NA	NA	NA	NA
189	Imazethapyr	81335-77-5	1.00E-04	-	NA	NA	NA	NA
190	Imidacloprid	138261-41-3	1.00E-04	-	NA	NA	NA	NA
191	Fenamiphos	22224-92-6	1.00E-04	-	NA	NA	NA	NA
192	Clopyralid	1702-17-6	1.00E-04	-	NA	NA	NA	NA
193	Metalaxyl	57837-19-1	1.00E-04	-	NA	NA	NA	NA
194	Monocrotophos	6923-22-4	1.00E-04	-	NA	NA	NA	NA
195	Indoxacarb	173584-44-6	8.00E-05	-	NA	NA	NA	NA
196	Acephate	30560-19-1	1.00E-04	-	NA	NA	NA	NA
197	Anilazine	101-05-3	1.00E-04*	-	NA	NA	NA	NA

198	Diuron	330-54-1	1.00E-04	-	NA	NA	NA	NA
199	Clofentezine	74115-24-5	1.00E-04*	-	NA	NA	NA	NA
200	Methamidophos	10265-92-6	1.00E-04	-	NA	NA	NA	NA
201	Thiamethoxam	153719-23-4	1.00E-04	-	NA	NA	NA	NA
202	Formetanate hydrochloride	23422-53-9	1.00E-04	-	NA	NA	NA	NA
203	Fluometuron	2164-17-2	1.00E-04	-	NA	NA	NA	NA
204	Difenzoquat metilsulfate	43222-48-6	1.00E-04	-	NA	NA	NA	NA
205	Bendiocarb	22781-23-3	1.00E-04	-	NA	NA	NA	NA
206	Alachlor	15972-60-8	1.00E-04	-	NA	NA	NA	NA
207	Dimethenamid	87674-68-8	1.00E-04	-	NA	NA	NA	NA
208	2,4-Dichlorophenoxyacetic acid	94-75-7	1.00E-04	-	NA	NA	NA	NA
209	Ethylene thiourea	96-45-7	1.00E-04	-	NA	NA	NA	NA
210	Azamethiphos	35575-96-3	1.00E-04	-	NA	NA	NA	NA
211	Dazomet	533-74-4	1.00E-04	-	NA	NA	NA	NA
212	Pyrimethanil	53112-28-0	1.00E-04	-	NA	NA	NA	NA
213	Propyzamide	23950-58-5	1.00E-04	-	NA	NA	NA	NA
214	Triadimenol	55219-65-3	1.00E-04	-	NA	NA	NA	NA
215	Pirimicarb	23103-98-2	1.00E-04	-	NA	NA	NA	NA
216	Isoxaben	82558-50-7	1.00E-04	-	NA	NA	NA	NA
217	Acetochlor	34256-82-1	1.00E-04	-	NA	NA	NA	NA
218	Acifluorfen	50594-66-6	1.00E-04	-	NA	NA	NA	NA
219	Tepraloxydim	149979-41-9	1.00E-04	-	NA	NA	NA	NA
220	Clopyralid-olamine	57754-85-5	1.00E-04	-	NA	NA	NA	NA
221	2,4-DB	94-82-6	1.00E-04	-	NA	NA	NA	NA
222	Hexazinone	51235-04-2	1.00E-04	-	NA	NA	NA	NA
223	Tebuthiuron	34014-18-1	1.00E-04	-	NA	NA	NA	NA
224	Iprodione	36734-19-7	1.00E-04	-	NA	NA	NA	NA
225	Dicamba	1918-00-9	1.00E-04	-	NA	NA	NA	NA
226	Methyl parathion	298-00-0	1.00E-04	-	NA	NA	NA	NA
227	Fluroxypyr	69377-81-7	1.00E-04	-	NA	NA	NA	NA
228	Dimethomorph	110488-70-5	1.00E-04	-	NA	NA	NA	NA
229	Benomyl	17804-35-2	1.00E-04	-	NA	NA	NA	NA
230	Monomethyl phthalate	4376-18-5	1.00E-04	-	NA	NA	NA	NA
231	Diazinon	333-41-5	1.00E-04	-	NA	NA	NA	NA
232	Cyclanilide	113136-77-9	1.00E-04	-	NA	NA	NA	NA
233	Cyanamide	420-04-2	1.00E-04	-	NA	NA	NA	NA
234	Ethoprop	13194-48-4	1.00E-04	-	NA	NA	NA	NA
235	Penoxsulam	219714-96-2	1.00E-04*	-	NA	NA	NA	NA
236	Clothianidin	210880-92-5	1.00E-04	-	NA	NA	NA	NA
237	Di(2-ethylhexyl) phthalate	117-81-7	1.00E-04	-	NA	NA	NA	NA
238	Acetamiprid	135410-20-7	1.00E-04	-	NA	NA	NA	NA
239	Novaluron	116714-46-6	1.00E-04*	-	NA	NA	NA	NA
240	Isoxaflutole	141112-29-0	1.00E-04	-	NA	NA	NA	NA
241	Imazamox	114311-32-9	1.00E-04	-	NA	NA	NA	NA
242	Sulfentrazone	122836-35-5	1.00E-04	-	NA	NA	NA	NA
243	Cyproconazole	94361-06-5	9.50E-05	-	NA	NA	NA	NA
244	Pymetrozine	123312-89-0	1.00E-04	-	NA	NA	NA	NA
245	Spiroxamine	118134-30-8	1.00E-04	-	NA	NA	NA	NA
246	Quinclorac	84087-01-4	1.00E-04	-	NA	NA	NA	NA
247	Triclopyr	55335-06-3	1.00E-04	-	NA	NA	NA	NA
248	Propamocarb hydrochloride	25606-41-1	1.00E-04	-	NA	NA	NA	NA
249	Monobutyl phthalate	131-70-4	1.00E-04	-	NA	NA	NA	NA
250	Pentachloronitrobenzene	82-68-8	1.00E-04	-	NA	NA	NA	NA
251	Flufenacet	142459-58-3	1.00E-04	-	NA	NA	NA	NA
252	Imazapyr	81334-34-1	1.00E-04	-	NA	NA	NA	NA
253	Trifloxysulfuron-sodium	199119-58-9	1.00E-04*	-	NA	NA	NA	NA
254	Propazine	139-40-2	1.00E-04	-	NA	NA	NA	NA

255	Thiacloprid	111988-49-9	1.00E-04	-	NA	NA	NA	NA
256	2-Methoxyethanol	109-86-4	1.00E-04	-	NA	NA	NA	NA
257	Chloridazon	1698-60-8	1.00E-04	-	NA	NA	NA	NA
258	Asulam	3337-71-1	1.00E-04	-	NA	NA	NA	NA
259	Pyrithiobac-sodium	123343-16-8	1.00E-04	-	NA	NA	NA	NA
260	Deisopropylatrazine	1007-28-9	1.00E-04	-	NA	NA	NA	NA
261	Molinate	2212-67-1	1.00E-04	-	NA	NA	NA	NA
262	Oxytetracycline dihydrate	6153-64-6	1.00E-04	-	NA	NA	NA	NA
263	Spirodiclofen	148477-71-8	1.00E-04	-	NA	NA	NA	NA
264	Carboxin	5234-68-4	1.00E-04	-	NA	NA	NA	NA
265	Oxamyl	23135-22-0	1.00E-04	-	NA	NA	NA	NA
266	Symclosene	87-90-1	1.00E-04	-	NA	NA	NA	NA
267	Fosthiazate	98886-44-3	1.00E-04	-	NA	NA	NA	NA
268	Sethoxydim	74051-80-2	1.00E-04	-	NA	NA	NA	NA
269	Dimethoate	60-51-5	1.00E-04	-	NA	NA	NA	NA
270	MCPA	94-74-6	1.00E-04	-	NA	NA	NA	NA
271	Paclobutrazol	76738-62-0	1.00E-04	-	NA	NA	NA	NA
272	Dipropyl 2,5-pyridinedicarboxylate	136-45-8	1.00E-04	-	NA	NA	NA	NA
273	Methyl isothiocyanate	556-61-6	1.00E-04	-	NA	NA	NA	NA
274	DEET	134-62-3	1.00E-04	-	NA	NA	NA	NA
275	Cyromazine	66215-27-8	1.00E-04	-	NA	NA	NA	NA
276	Imazaquin	81335-37-7	1.00E-04	-	NA	NA	NA	NA
277	Metribuzin	21087-64-9	1.00E-04	-	NA	NA	NA	NA
278	Flumetsulam	98967-40-9	1.00E-04	-	NA	NA	NA	NA
279	Triadimefon	43121-43-3	1.00E-04	-	NA	NA	NA	NA
280	Metolachlor	51218-45-2	1.00E-04	-	NA	NA	NA	NA
281	Permethrin	52645-53-1	1.00E-04	-	NA	NA	NA	NA
282	Terbacil	5902-51-2	1.00E-04	-	NA	NA	NA	NA
283	Triadimenol	55219-65-3	1.00E-04	-	NA	NA	NA	NA
284	Etridiazole	2593-15-9	1.00E-04	-	NA	NA	NA	NA
285	Propoxycarbazone-sodium	181274-15-7	1.00E-04	-	NA	NA	NA	NA
286	Mevinphos	7786-34-7	1.00E-04	-	NA	NA	NA	NA
287	Bromacil	314-40-9	1.00E-04	-	NA	NA	NA	NA
288	Metam-sodium hydrate	6734-80-1	1.00E-04	-	NA	NA	NA	NA
289	2,4-Dichlorophenoxyacetic acid	94-75-7	1.00E-04	-	NA	NA	NA	NA
290	Thiabendazole	148-79-8	1.00E-04	-	NA	NA	NA	NA
291	Atrazine	1912-24-9	1.00E-04	-	NA	NA	NA	NA
292	2-Phenoxyethanol	122-99-6	1.00E-04	-	NA	NA	NA	NA
293	Icaridin	119515-38-7	1.00E-04	-	NA	NA	NA	NA
294	Imazapic	104098-48-8	1.00E-04	-	NA	NA	NA	NA
295	Aldicarb	116-06-3	1.00E-04	-	NA	NA	NA	NA
296	Triticonazole	131983-72-7	9.50E-05	-	NA	NA	NA	NA
297	Diazoxon	962-58-3	1.00E-04	-	NA	NA	NA	NA
298	Maleic hydrazide	123-33-1	1.00E-04	-	NA	NA	NA	NA
299	Daminozide	1596-84-5	1.00E-04	-	NA	NA	NA	NA
300	Mepiquat chloride	24307-26-4	1.00E-04	-	NA	NA	NA	NA
301	Norflurazon	27314-13-2	1.00E-04	-	NA	NA	NA	NA
302	Chloroneb	2675-77-6	1.00E-04	-	NA	NA	NA	NA
303	Ethephon	16672-87-0	1.00E-04	-	NA	NA	NA	NA
304	Iodosulfuron-methyl-sodium	144550-36-7	1.00E-04	-	NA	NA	NA	NA
305	Simazine	122-34-9	1.00E-04	-	NA	NA	NA	NA
306	MEHP	4376-20-9	1.00E-04	-	NA	NA	NA	NA
307	Cymoxanil	57966-95-7	1.00E-04	-	NA	NA	NA	NA
308	Diquat dibromide monohydrate	6385-62-2	5.00E-05	-	NA	NA	NA	NA
309	Dimethyl phthalate	131-11-3	1.00E-04	-	NA	NA	NA	NA
310	Dichlobenil	1194-65-6	1.00E-04	-	NA	NA	NA	NA

Table 3. Summary of assay performance metrics for single-concentration and multi-concentration screening.

Assay[1]	CV of DMSO		Z' Score		AC50 of positive control[2]	
	mean±SD	range	mean±SD	range	mean±SD	range
Single-con RAIU	7.14% ± 1.56%	4.91% - 11.04%	0.77 ± 0.05	0.65 - 0.84	-6.44 ± 0.11	-6.56 - -6.06
Multi-con RAIU	8.61% ± 1.01%	6.70 - 11.50	0.72 ± 0.03	0.64 - 0.78	-6.38 ± 0.13	-6.57 - -6.04
Multi-con Cell Viability	5.42% ± 1.47%	2.80 - 9.53	n.a.	n.a.	-4.83 ± 0.12	-4.92 - -4.47

1: All metrics were calculated per assay plate (single-con: n=15, multi-con: n=54) and summarized separately for single-concentration and multi-concentration screenings.

2: AC50 of positive controls were calculated from the dose-responses of $NaClO_4$ and DCNQ for RAIU and cell viability assay respectively. Unit: logM.

n.a.: unable to calculate.

Table 4. Summary of normalized responses of control chemicals across all plates

Assay[1]	DMSO	2,4-D	DCNQ[2] (1E-4M)	$NaClO_4$[2] (1E-4M)	$NaNO_3$	NaSCN
single-con RAIU	100.63 ± 7.11	92.41 ± 4.24	n.a.	2.85 ± 0.36	81.25 ± 7.56	20.64 ± 1.12
multi-con RAIU	99.5 ± 8.28	90.86 ± 4.49	3.92 ± 3.37	3.28 ± 0.38	83.08 ± 7.17	24.69 ± 2.71
multi-con Cell Viability	100.92 ± 5.41	99.34 ± 3.21	3.72 ± 0.38	99.19 ± 4.69	98.95 ± 5.43	104.3 ± 3.98

Mean ± S.D.

n.a.: not available as DCNQ was not included in the single-concentration screening.

1. Data were calculated by collecting normalized response for each chemical from all assay plates. Values represent the percent of control activity. 2,4-D, $NaNO_3$, and NaSCN were at a concentration of 100 μM.

2. For DCNQ and $NaClO_4$, though they were included on each assay plate in six concentrations, only the responses from 100 μM concentration are summarized in this table.

NHEERL Fact Sheet

High-Throughput Screening of ToxCast Phase I Chemical Library for Sodium Iodide Symporter (NIS) Inhibitors

To be submitted to *Toxicological Sciences*

Jun Wang[1,2], Daniel R. Hallinger[1], Ashley S. Murr[1], Angela R. Buckalew[1], Steven O. Simmons[3], Tammy E. Stoker[1], and Susan C. Laws.[1]

[1]Endocrine Toxicology Branch, Toxicity Assessment Division, National Health and Environmental Effects Research Laboratory, ORD, U.S.EPA, Research Triangle Park, NC.
[2]Oak Ridge Institute for Science and Education, US Dept. of Energy, Oak Ridge, TN 37831.
[3]National Center for Computational Toxicology, ORD, U.S.EPA, Research Triangle Park, NC.

Relevant National Research Program project/area of research: This paper supports Chemical Safety for Sustainability (CSS) research on High Throughput Toxicology, CSS 16.01, Task 2.1, *Development and optimization of vitro assays to address EDSP chemical activity toward targets affecting thyroid hormone,* Milestone 2. *Development of a Thyroid Sodium Iodide Symporter (NIS) Assay.*

Impact Statement: A novel screening approach has been developed to rapidly identify chemicals that can inhibit the uptake of iodide by the thyroid and disrupt the synthesis of thyroid hormones. This work addressed an urgent need and request from the Office of Coordination and Science Policy to develop *in vitro* assays to detect potential thyroid toxicants, and now provides a rapid screening approach that targets a key molecular initiating event, the uptake of iodide as mediated by the thyroid sodium iodide symporter (NIS), within the thyroid hormone pathway. This assay was used to screen the ToxCast Phase 1 chemical library. These findings for the Phase1-v2 chemicals can be utilized during an upcoming 2018 FIFRA Science Advisory Panel review to obtain recommendations and feedback for the Agency's Endocrine Disrupting Screening Program regarding the appropriate use of high throughput in vitro assays for the thyroid hormone pathway. This work is also of international interest because of the novel cell line created for this RAIU assay and its potential use for the development of an OECD test guideline.

Background: The Agency's Endocrine Disruptor Screening Program in the 21st century (EDSP21) aims to use high-throughput and computational toxicology methods to screen and prioritize chemicals for further testing based on their potential to affect estrogen, androgen, and thyroid pathways ([HYPERLINK "https://www.epa.gov/endocrine-disruption"]). The EDSP21 is currently limited in the ability to screen for chemicals that have the potential to affect homeostasis of the thyroid hormone signaling pathway. The development of the thyroid sodium/iodide symporter (NIS) assay is part of an effort lead by the Office of Research and Development to counteract this limitation by developing medium- and high-throughput screening assays that focus on molecular initiating events that could ultimately affect circulating thyroid hormone levels. To maintain sufficient concentrations of circulating thyroid hormones, the thyroid requires the active uptake of iodide as mediated by the NIS. Monovalent anions, such as the environmental contaminant perchlorate, have been well characterized as competitive inhibitors of NIS-mediated uptake of iodide, but limited information exists for more structurally diverse chemicals. The development of a screening approach to identify NIS inhibitors will enable the rapid prioritization of chemicals currently under the Agency's purview for further testing as potential thyroid disrupting activity.

Study Description: A novel cell line stably expressing human sodium iodide symporter (NIS), hNIS-HEK293T-EPA, was developed for use in a screening approach to identify chemicals that inhibit NIS-

mediated radioactive iodide uptake (RAIU). For this RAIU assay, NIS-expressing cells were exposed to ^{125}I in the presence of serial dilutions of each test chemical ranging from 0.001 – 100mM. NIS-mediated ^{125}I uptake was then quantified to identify test chemicals that inhibit this action, indicated by decreased intracellular ^{125}I uptake relative to controls. Experiments were conducted to determine optimized assay conditions and to demonstrate assay performance using a set of reference chemicals containing known inhibitors of NIS-mediated iodide uptake and known inactive chemicals. This assay was used to screen chemicals in the ToxCast Phase 1_v2 chemical library for the potential to inhibit thyroid hormone synthesis by disrupting the NIS. A cell viability assay was subsequently conducted for each chemical used in the RAIU assay. A ranking system was developed based on the multi-concentration responses in the NIS assay and the confounding cytotoxicity for the 293 chemicals to inform the prioritization of the chemicals for secondary testing.

Research Results: Results from this study demonstrated that the NIS-mediated ^{125}I uptake assay is accurate, reproducible, and reliable for screening large libraries of chemicals. The ranking scores were assigned to chemicals which inhibited the NIS activity by more than 50% and allowed selection of chemicals with the potential to interfere with thyroid synthesis. Based on the ranking of the positives in the multi-concentration testing, approximately 21 of the 293 are being tested in follow-up secondary assays to confirm inhibitory activity.

Conclusion: The use of hNIS-HEK293T-EPA cells in the NIS-mediated iodide uptake and cell viability assays provide the U.S.EPA with a rapid approach for identifying chemicals that have the potential to disrupt a key molecular step essential for the synthesis of thyroid hormones. The screening and ranking of 293 chemicals in this study represents the first large scale effort to investigate NIS as a molecular target of environmental chemicals that covers a broad spectrum of structural and toxicological properties. These data can inform the prioritization of chemicals for secondary testing, and support the needs of the Endocrine Disruptor Screening Program for additional high-throughput in vitro assays to screen chemicals for interaction with more molecular targets that can disrupt normal thyroid hormone signaling. This assay and ranking approach can now be used for screening other larger chemical libraries such as the ToxCast Phase1_v2, Phase 2, and E1K libraries.¶

Contact: Tammy Stoker, Ph.D., [HYPERLINK "mailto:Stoker.Tammy@epa.gov"] (919) 541-2783 or Susan Laws, Ph.D., [HYPERLINK "mailto:Laws.Susan@epa.gov"] (919) 541-0173, Endocrine Toxicology Branch, Toxicity Assessment Division, NHEERL, ORD, U.S. EPA.

Message

From: Wadlington, Christina [Wadlington.Christina@epa.gov]
Sent: 7/6/2017 12:00:55 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: MCLG.Perchlorate Roll Out_5.15.17.docx
Attachments: MCLG.Perchlorate Roll Out_5.22.17_SenttoOW.DOCX

Hello! The one I sent up is attached.

From: Christ, Lisa
Sent: Thursday, July 06, 2017 7:59 AM
To: Wadlington, Christina <Wadlington.Christina@epa.gov>
Subject: FW: MCLG.Perchlorate Roll Out_5.15.17.docx

Hi – just want to confirm this is the current version…
Lisa

From: Christ, Lisa
Sent: Tuesday, May 30, 2017 9:44 AM
To: Wadlington, Christina <Wadlington.Christina@epa.gov>
Cc: Burneson, Eric <Burneson.Eric@epa.gov>; Gonzalez, Yvonne V. <Gonzalez.Yvonne@epa.gov>; Mclain, Jennifer <Mclain.Jennifer@epa.gov>; Olson, Daniel <Olson.Daniel@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: MCLG.Perchlorate Roll Out_5.15.17.docx

Hi Christina,
I'm okay with the changes and replied in the comment bubbles to questions.
Lisa

From: Wadlington, Christina
Sent: Tuesday, May 30, 2017 8:09 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Burneson, Eric <Burneson.Eric@epa.gov>; Gonzalez, Yvonne V. <Gonzalez.Yvonne@epa.gov>; Mclain, Jennifer <Mclain.Jennifer@epa.gov>
Subject: RE: MCLG.Perchlorate Roll Out_5.15.17.docx

Morning!

I updated this document to address Jennifer's comment where I could.
Can you take a look at the rest and let me know if they are ok?

From: Mclain, Jennifer
Sent: Tuesday, May 30, 2017 8:00 AM
To: Wadlington, Christina <Wadlington.Christina@epa.gov>
Cc: Gonzalez, Yvonne V. <Gonzalez.Yvonne@epa.gov>; Grevatt, Peter <Grevatt.Peter@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Subject: Fwd: MCLG.Perchlorate Roll Out_5.15.17.docx

Christina
A few comments on the perchlorate comm plan. Let me know if you want to discuss.
Thanks!
Jennifer

Message

From: Olson, Daniel [Olson.Daniel@epa.gov]
Sent: 5/8/2017 3:37:08 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
CC: Miller, Gregory [Miller.Gregory@epa.gov]
Subject: FW: Perchlorate FRNs and Transmittal
Attachments: 2016-action-information-template.doc; DRAFT Perchlorate Action Information 05-08-17V2.doc

Lisa,

Please find attached for your review the draft Action Information one-pager (2.5 pages) based on the attached template Steph sent.

Thanks,

Dan

From: Flaharty, Stephanie
Sent: Friday, May 05, 2017 11:05 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>; Olson, Daniel <Olson.Daniel@epa.gov>
Cc: Miller, Gregory <Miller.Gregory@epa.gov>
Subject: FW: Perchlorate FRNs and Transmittal

Dan,

I concluded my initial review of the FRNs (see attached mark-ups).

Thanks,
Steph

From: Flaharty, Stephanie
Sent: Friday, May 05, 2017 8:16 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>; Olson, Daniel <Olson.Daniel@epa.gov>
Cc: Miller, Gregory <Miller.Gregory@epa.gov>
Subject: RE: Perchlorate FRNs and Transmittal

Dan,

I'll do an initial review of the FRNs this morning. In the meantime, we need to draft an action information one pager to submit to OW as soon as possible (see template attached). The one-pager will suffice for both FRNs.

Thx,
Steph

From: Christ, Lisa
Sent: Wednesday, May 03, 2017 4:50 PM
To: Olson, Daniel <Olson.Daniel@epa.gov>
Cc: Miller, oGregory <Miller.Gregory@epa.gov>; Flaharty, Stephanie <Flaharty.Stephanie@epa.gov>
Subject: RE: Perchlorate FRNs and Transmittal

Dan,

Attached are my comments on the 2 FRNs and memo. I'm including Stephanie on this email so she can do a preliminary review to expedite things later on.

For the memo, you will need 2; one from Eric to Peter and another from Peter to Mike – the content will be similar.
Lisa

From: Olson, Daniel
Sent: Tuesday, May 02, 2017 9:41 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Miller, Gregory <Miller.Gregory@epa.gov>
Subject: Perchlorate FRNs and Transmittal

Lisa,

Please find attached for your review two FRNs and a transmittal memo from Eric to Mike:

- The draft MCLG approach and revised draft model (45 day comment period, comments sent to EPA)
- List of peer reviewers and draft charge questions (21 day comment period, comments sent to Versar)

Thanks,

Dan

Message

From: Lan, Alexis [lan.alexis@epa.gov]
Sent: 6/2/2020 7:53:22 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]; Albert, Ryan [Albert.Ryan@epa.gov]
CC: Khera, Rajiv [Khera.Rajiv@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]
Subject: FW: Internal Agency review of the PFBS Toxicity Assessment - link to review materials and logistics
Attachments: Response to Peer Review 2 Comments on PFBS Toxicity Assessment.docx; DRAFT Interagency and Agency Tox Assessment for PFBS_May 2020.docx

Good afternoon Lisa and Ryan,

Thank you both for chatting earlier. Please see the message from Greg Miller below. I suspect that Crystal, Eric and Jennifer will also want to review and provide feedback. To facilitate those reviews in time, here is what I propose in terms of next steps:

- Provide staff-level (SRRB/TAB) comments to Lisa and Ryan by **COB Tuesday 6/9**
- Lisa and Ryan to review and provide comments to Crystal and/or Eric by **Tuesday 6/16**
- Transmit consolidated SRMD comments to Jennifer by **Tuesday 6/23**

I'll be happy to coordinate and consolidate comments during this process. Please let me know if you have any questions or concerns, and thank you in advance for your time on this review.

All the best,

Alex Lan, MPH
Physical Scientist
Office of Ground Water and Drinking Water
Standards and Risk Management Division
U.S. Environmental Protection Agency
Washington, D.C.
Lan.Alexis@epa.gov
(Desk) 202.564.0841
(Mobile) 703.303.7791

From: Miller, Gregory <Miller.Gregory@epa.gov>
Sent: Tuesday, June 02, 2020 2:45 PM
To: Lan, Alexis <lan.alexis@epa.gov>
Cc: Strong, Jamie <Strong.Jamie@epa.gov>; Behl, Betsy <Behl.Betsy@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Subject: FW: Internal Agency review of the PFBS Toxicity Assessment - link to review materials and logistics

Hi Alex,
Attached you will find the PFBS Toxicity Assessment that is being shared for internal EPA review through the usual IRIS process. I'm sharing these documents with you as the point of contact for OGWDW. Jennifer McLain has flagged the thyroid (email below) as an area of concern given the perchlorate NPDWS rule withdrawal currently under review at OMB. Please coordinate your response with the perchlorate team in OGWDW (Sam, Rajiv, Lisa) as you draft your comments. Comments are due to ORD by 6/30, but if you could have your comments to me by 6/25, I will combine the OST and OGWDW comments into one document as was requested.

Thanks!

Greg Miller, Senior Environmental Health Scientist
Team Lead, Human Health Risk Assessment Branch
Office of Science and Technology, Health and Ecological Criteria Division
US Environmental Protection Agency, Office of Water
1200 Pennsylvania Ave, NW (MC 4304T)
Washington, DC 20460

phone: (202) 566-2310

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Monday, June 01, 2020 11:31 AM
To: Behl, Betsy <Behl.Betsy@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>
Subject: PFBS assessment

Betsy – you may already be doing this but I wanted to make sure we are connected to ORD as they respond to their peer review comment: Need for additional clarifying language on the physiology and function of thyroid hormones during pregnancy and further description of the clinical condition "hypothyroxinemia". I'm reviewing the perchlorate response to comment document now and just want to make sure we are being consistent.

Thanks
Jennifer

From: Jones, Samantha <Jones.Samantha@epa.gov>
Sent: Monday, June 1, 2020 5:34 PM
To: Cassidy, Meghan <Cassidy.Meghan@epa.gov>; Olsen, Marian <Olsen.Marian@epa.gov>; Rogers, Rick <rogers.rick@epa.gov>; Gehlhaus, Martin <Gehlhaus.Martin@epa.gov>; Allenbach, Becky <Allenbach.Becky@epa.gov>; Pollard, Solomon <Pollard.Solomon@epa.gov>; Adams, Glenn <Adams.Glenn@epa.gov>; Harris, Kimberly <harris.kimberly@epa.gov>; Mangino, Mario <mangino.mario@epa.gov>; Morton, Michael <Morton.Michael@epa.gov>; Milburn, Anna <Milburn.Anna@epa.gov>; Wooster-Brown, Catherine <Wooster-Brown.Catherine@epa.gov>; Schumacher, Kelly <Schumacher.Kelly@epa.gov>; Bahrman, Sarah <Bahrman.Sarah@epa.gov>; Benson, Bob <Benson.Bob@epa.gov>; Small, Matthew <Small.Matthew@epa.gov>; Stralka, Daniel <Stralka.Daniel@epa.gov>; Allen, Elizabeth <allen.elizabeth@epa.gov>; Anderson-Carnahan, Linda <Anderson-Carnahan.Linda@epa.gov>; Miller, Gregory <Miller.Gregory@epa.gov>; Lowit, Anna <Lowit.Anna@epa.gov>; Barone, Stan <Barone.Stan@epa.gov>; Hamernik, Karen <Hamernik.Karen@epa.gov>; Raffaele, Kathleen <raffaele.kathleen@epa.gov>; Murphy, Deirdre <Murphy.Deirdre@epa.gov>; Vasu, Amy <Vasu.Amy@epa.gov>; Hoyer, Marion <hoyer.marion@epa.gov>; Axelrad, Daniel <Axelrad.Daniel@epa.gov>; Dzubow, Rebecca <Dzubow.Rebecca@epa.gov>; Lloyd, Christine <Lloyd.Christine@epa.gov>
Cc: Owens, Beth <Owens.Beth@epa.gov>; Lambert, Jason <Lambert.Jason@epa.gov>; Shams, Dahnish <Shams.Dahnish@epa.gov>
Subject: Internal Agency review of the PFBS Toxicity Assessment - link to review materials and logistics

Hello all,

You are receiving this email because you have been identified as your office's point of contact for review of toxicity assessments in general and/or as the PFAS point of contact. If this has reached you by mistake and there is another individual that should be the point person, please let me know as soon as you can.

This email is to initiate the internal agency review of the revised PFBS toxicity assessment. Shortly, you will be granted access to the SharePoint site (see link below) so that you will be able to obtain the PFBS draft toxicity assessment as well as the Response to peer review comments document. Please feel free to circulate the materials within your respective

office, we just ask that as the points of contact, that you compile and upload one set of comments from your respective office. We request that you post comments to the SharePoint site by **COB Tuesday, June 30th**.

https://usepa.sharepoint.com/sites/ORD_Work/pfas_toxval_internal_review/SitePages/Home.aspx

We appreciate your feedback. Please let me know if there are any questions.

Thank you!
Samantha

Samantha J. Jones, PhD
Associate Director, Center for Public Health and Environmental Assessment (CPHEA)
National Program Director, Health and Environmental Risk Assessment (HERA) Research Program
Office of Research and Development (ORD)
US Environmental Protection Agency (EPA)
RRB 71210, Washington, DC
(o) 202-564-6794; (m) 703-943-7990

Appointment

From: ONeill, Sandra [ONeill.Sandra@epa.gov]
Sent: 3/17/2017 8:33:23 PM
To: Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]; Regli, Stig [Regli.Stig@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]

Subject: Pre-meet: OPP/CI Chlorate and Perchlorate Follow-up Discussion
Attachments: 2017 CI Comment Letter on Perchlorate.pdf; PDF Perchlorate Isotope Study.pdf; Agenda for OPP-CI Chlorate-Perchlorate Follow-Up Meeting 3-23-17.docx
Location: DCRoomPYS8100/Potomac-Yard-One

Start: 3/20/2017 6:00:00 PM
End: 3/20/2017 7:00:00 PM
Show Time As: Tentative

<!--[if lte mso 15 || CheckWebRef]-->

ONeill, Sandra has shared a OneDrive for Business file with you. To view it, click the link below.

Hypochlorite Best Management Practices 3-17-17.docx

<!--[endif]-->

Call in: Ex. 6 Personal Privacy (PP) if in the office or Ex. 6 Personal Privacy (PP) if outside the office
Conference Extension: Ex. 6 Personal Privacy (PP)
Participant Code: Ex. 6 Personal Privacy (PP)

Hypochlorites team,

Since our 1-24-17 meeting with the Chlorine Institute (CI), CI has submitted comments on chlorate and perchlorate that may have an impact on our path forward. We've also identified best management practices from OW, AWWA, and the Chlorine Institute. Our next meeting with CI is on Thursday, 3-23-17.

By the end of this meeting, we want to:

1.) Review comments from CI
2.) Review the BMPs comparison document, are there any BMPs we wouldn't consider?
3.) Finalize agenda for 3-23-17 meeting

Please see the following documents:

1.) CI Comment Documents
    a. CI Comment Letter on Perchlorate: reaffirms that AWWA reports predate 1-1-13 implementation of NSF/ANSI Standard 60 and don't reflect perchlorate minimization improvements, perchlorate levels are likely more from naturally occurring chlorate, and a 2016 isotope study (also attached) provides compelling evidence that natural perchlorate is the dominant source of human exposure.
    b. 2017 CI Comment Letter on NRDC Recommendations: CI negates use of pH as a BMP, and various other non-BMP related issues.
2.) Hypochlorite Best Management Practices 3-17-17: compares BMPs from AWWA, CI, and OW.
3.) Agenda for OPP-CI Chlorate-Perchlorate Follow-Up Meeting 3-23-17 (they will be calling in), this agenda is a draft.

Thank you all!

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 3/30/2017 12:30:00 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Materials needed
Attachments: One_pager_Perchlorate in drinking water_fv_32217.doc

Here is what the IO has

From: Gonzalez, Yvonne V.
Sent: Thursday, March 30, 2017 8:24 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>
Subject: RE: Materials needed

Eric,

The one-pager prepared by your team might be useful.

Regards,
Yvonne-Veronica Gonzalez
Special Assistant (on detail)
Office of Ground and Drinking Water
U.S. Environmental Protection Agency
(202)564-2912

From: Grevatt, Peter
Sent: Thursday, March 30, 2017 8:20 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>
Cc: Gonzalez, Yvonne V. <Gonzalez.Yvonne@epa.gov>; Ruf, Christine <Ruf.Christine@epa.gov>
Subject: FW: Materials needed

FYI. Can you two connect and determine the best off-the-shelf product for us to send up?

From: Best-Wong, Benita
Sent: Thursday, March 30, 2017 7:46 AM
To: Grevatt, Peter <Grevatt.Peter@epa.gov>
Cc: Ruf, Christine <Ruf.Christine@epa.gov>
Subject: Materials needed

Peter,
As a follow up from Mike's general with Sarah yesterday, she would like a background paper on perchlorate. I'm hoping that you have something already prepared that I can provide to her. I'm also copying Christine in case she has something already available.
Benita

Benita Best-Wong
Acting Deputy Assistant Administrator
Office of Water
US EPA
1200 Pennsylvania Avenue, NW
Washington, DC 20460

202-566-1159

Message

From: Townsend, Clifton [Townsend.Clifton@epa.gov]
Sent: 2/28/2017 8:25:34 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Hey!
Attachments: PerchlorateOccMonitoringReport_Revised Clean 2013.docx

From: Townsend, Clifton
Sent: Wednesday, February 15, 2017 11:03 AM
To: El-Burai-Felix, Alia <el-burai-felix.alia@epa.gov>
Subject: RE: Hey!

Thank you so much. Attached you will see the Perchlorate occ report that was updated to 2013 for your review.

Talk with you shortly

Clifton

Clifton C. Townsend, MSPH
Environmental Scientist
U.S. Environmental Protection Agency
Office of Ground Water and Drinking Water
Targeting and Analysis Branch
Phone: 202-564-1576 Fax: 202-564-3760 MC: 4607
E-mail: townsend.clifton@epa.gov

From: El-Burai-Felix, Alia
Sent: Wednesday, February 15, 2017 10:56 AM
To: Townsend, Clifton <Townsend.Clifton@epa.gov>
Subject: Hey!

Hi, Clifton!

Best regards,

Alia El Burai Félix, MS
Physical Scientist
Targeting and Analysis Branch
Standards and Risk Management Division
Office of Groundwater and Drinking Water
U.S. Environmental Protection Agency
EPA East Bldg. Rm. 2357G
Office phone number: 202-566-2572

Message

From: Huff, Lisa [Huff.Lisa@epa.gov]
Sent: 2/21/2017 3:23:30 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Perchlorate occ doc
Attachments: POMR with chamber options.pptx

Flag: Follow up

Lisa,
Attached is the draft ppt from Clif on perchlorate occurrence – he said that he would like to go through it with you and get your feedback so I suggested he go ahead and find a time on your calendar and to invite Dan as well.

Thanks,

Lisa Foersom Huff

Associate Branch Chief
Targeting and Analysis Branch
Standards and Risk Management Division
Office of Groundwater and Drinking Water
U.S. EPA
EPA East Bldg. Rm. 2357 H
202-566-0787

From: Townsend, Clifton
Sent: Tuesday, February 21, 2017 10:04 AM
To: Huff, Lisa <Huff.Lisa@epa.gov>
Subject: RE: Perchlorate occ doc

Hi Lisa,

Attached is the electronic version of the draft briefing on the Perchlorate Occurrence Report. I will find a time for us (You , Dan and Lisa) to meet and discuss further.

Clifton

From: Huff, Lisa
Sent: Tuesday, February 21, 2017 9:47 AM
To: Townsend, Clifton <Townsend.Clifton@epa.gov>
Subject: RE: Perchlorate occ doc

Clif,
Did you send me the electronic version of your briefing? I couldn't find one so if you would please send that to me I'd appreciate it. Also as far as next steps and timing I wasn't sure if you needed or were waiting for direction or input from Lisa on how Cadmus should proceed with updating the occurrence doc? It might be good to set up a time to go over the briefing with Lisa and Dan so they can understand any issues or concerns you might have on updating the occurrence doc – I would like to be included but I think it might be difficult for me to relay any issues or provide you with specific recommendations based on my limited involvement on this project.

Thanks,

Lisa Foersom Huff

Associate Branch Chief
Targeting and Analysis Branch
Standards and Risk Management Division
Office of Groundwater and Drinking Water
U.S. EPA
EPA East Bldg. Rm. 2357 H
202-566-0787

From: Townsend, Clifton
Sent: Tuesday, February 14, 2017 4:31 PM
To: Huff, Lisa <Huff.Lisa@epa.gov>
Subject: Perchlorate occ doc

Hi Lisa,

Attached is the Perchlorate Occurrence Report that is current till 2013. Per our pre brief this will give some additional background and perspective on where the Office was in our attempt to start the NPDWR for perchlorate.

Thank you again for going over the briefing with me as well.

Clifton

Clifton C. Townsend, MSPH
Environmental Scientist
U.S. Environmental Protection Agency
Office of Ground Water and Drinking Water
Targeting and Analysis Branch
Phone: 202-564-1576 Fax: 202-564-3760 MC: 4607
E-mail: townsend.clifton@epa.gov

Message

From: Perkinson, Russ [Perkinson.Russ@epa.gov]
Sent: 1/19/2017 1:35:43 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Pre-Meeting comments
Attachments: Pre-Meeting Comment Report for Perchlorate.docx; List of Registered Observers for Perchlorate.pdf

The Word doc has the pre-meeting comments.

From: Perkinson, Russ
Sent: Thursday, January 05, 2017 6:50 AM
To: Olson, Daniel <Olson.Daniel@epa.gov>
Cc: Christ, Lisa <christ.lisa@epa.gov>
Subject: FW: Pre-Meeting comments

Dan – FYI, here's the pre-meeting comments from peer reviewers. I haven't looked over them and probably won't in any detail, so hoping you can.
Thanks,
Russ

From: Riley, Karie [mailto:KRiley@versar.com]
Sent: Wednesday, January 04, 2017 5:45 PM
To: Perkinson, Russ <Perkinson.Russ@epa.gov>
Subject: Pre-Meeting comments

Hi Russ,

Please find attached the pre-meeting comments and list of observers. We have sent these and the agenda to the reviewers.

Karie

Karie Riley
Environmental Services Group
Versar, Inc.
6850 Versar Center
Springfield, VA 22151
Direct Line: (703) 642-6915
Fax: (703) 642-6809
Email: kriley@versar.com
Visit us at: www.versar.com

External Peer Review Meeting for EPA's
Draft Biologically Based Dose-Response (BBDR) Model and Draft BBDR Model Report for Perchlorate in Drinking Water

Crystal City Marriott at Reagan National Airport
1999 Jefferson Davis Highway
Arlington, VA, 22202

January 10 and 11, 2017

LIST OF REGISTERED OBSERVERS

Eileen Abt (on phone)
U.S. FDA/CFSAN

Erica Bernstein
The Chlorine Institute

Thomas D. Blackman
Lockheed Martin Corporation

Lauren Brown
Abt Associates

Eric Burneson
U.S. EPA

Lisa Christ
U.S. EPA

Lisa Corey
Intertox

William S. Eck (on phone)
U.S. Army Public Health Center

Jeff Fisher
U.S. FDA

Lynn Flowers
U.S. EPA

Jessica Georges
U.S. EPA

Mark Gibson
American Chemistry Council

Peter Grevatt
U.S. EPA

Ahmed Hafez
U.S. EPA

Erik Helm
U.S. EPA

Sam Hernandez
U.S. EPA

John Herrmann (on phone)
Policy Navigation Group

Caryn Kelly (on phone)
Amec Foster Wheeler

Jonathan Koplos (on phone)
The Cadmus Group, Inc.

Jason Leuck
Lockheed Martin Corporation

Bruce Maclear (on phone)
U.S. EPA Region 9

Greg Miller (on phone)
U.S. EPA

Kevin M. Morley (comments)
American Water Works Association

Mary P. Morningstar
Lockheed Martin Corporation

Daniel Olson
U.S. EPA

Sandra O'Neill
U.S. EPA

Darrell Osterhoudt
Association of State Drinking Water Administrators

Russ Perkinson
U.S. EPA

Richard Pleus (comments)
Intertox

Jim Rollins
Policy Navigation Group

Paul Schlosser
U.S. EPA

David Schultz
Bloomberg BNA

Steve Shost
NYS Department of Health

Clifton Townsend
U.S. EPA

Shradha Upadhayay (on phone)
Metropolitan Water District of Southern California

Linda M. Wilson (on phone)
NYS Office of the Attorney General

DRAFT
Pre-Meeting Peer Review Summary Report

External Peer Review for EPA's *Draft Biologically Based Dose-Response (BBDR) Model and Draft BBDR Model Report for Perchlorate in Drinking Water*

January 4, 2017

Peer Reviewers:

Hugh A. Barton, Ph.D.
Claude Emond, Ph.D.
Dale Hattis, Ph.D.
Angela M. Leung, M.D., M.Sc.
Michael Lumpkin, Ph.D., DABT
Elizabeth N. Pearce, M.D., M.Sc.
Stephen M. Roberts, Ph.D.
Joanne F. Rovet, Ph.D.

Contract No. EP-C-13-010
Task Order 2015-22

Prepared for:
U.S. Environmental Protection Agency
Office of Ground Water and Drinking Water,
Standards and Risk Management Division,
1200 Pennsylvania Avenue NW (MC 4607M)
Washington, DC 20460

Prepared by:
Versar, Inc.
6850 Versar Center
Springfield, VA 22151

TABLE OF CONTENTS

[TOC \o "1-3" \h \z \u]

I. BACKGROUND

The U.S. EPA's Office of Water is in the process of developing National Primary Drinking Water Regulations for perchlorate under the Safe Drinking Water Act. In 2012, EPA submitted a white paper *Life Stage Considerations and Interpretation of Recent Epidemiological Evidence to Develop a Maximum Contaminant Level Goal for Perchlorate* (U.S. EPA, 2012) to the Science Advisory Board (SAB) for review. The white paper presented scientific information published since the National Research Council (NRC) released their 2005 Report "Health Implications of Perchlorate Ingestion" and described how EPA derived a range of Maximum Contaminant Level Goal (MCLG) values for life stages of concern. In their 2013 report, the SAB concluded that EPA should: 1) consider exposure to the following sensitive life stages: the fetuses of hypothyroxinemic pregnant women and infants exposed to perchlorate through either water-based formula or the breast milk of lactating women, and 2) derive the MCLG using a physiologically-based pharmacokinetic/pharmacodynamic (PBPK/PD) model to account for exposure differences and biological differences across life stages, including sensitive life stages. Specifically, the SAB found that the 'default algebraic approach provides limited ability to address the various exposure and biological factors affecting sensitivity to perchlorate at different life stages.' The SAB concluded that from a scientific standpoint it would be more appropriate to base the MCLG derivation on the perchlorate mode of action, using PBPK/PD modeling to relate perchlorate concentrations in drinking water to biological effects rather than the default approach.

The SAB report referenced a report by Lumen et al. (2013) on the effect of perchlorate on thyroid hormone perturbations for pregnant mothers and fetuses, as well as their work to extend a physiologically-based pharmacokinetic/pharmacodynamic iodine uptake inhibition (PBPK/PD-IUI) model with links to serum thyroid hormone levels, as a starting point for EPA's efforts.

The new modeling effort presented here integrates the previous EPA PBPK model (2009) for perchlorate with the model developed by Lumen et al. (2013) for pregnant mothers and fetuses (humans) and iodide models developed by Fisher et al. (2013) for lactating rats and Fisher et al. (2016) for lactating mothers and nursing infants (humans). The model has been subjected to a quality assurance (QA) review that was conducted by Oak Ridge National Laboratory (data and parameters used) and Pacific Northwest National Laboratory (model code). The Biologically Based Dose Response (BBDR) model predicts thyroid hormone perturbations for lactating mothers, breast-fed infants and bottle-fed infants resulting from exposure to perchlorate under different dietary iodine intake levels. EPA is relying on the Lumen et al. (2013) model, peer reviewed and published previously, to predict effects for pregnant mothers and fetuses. It is important to note a modification to a key parameter was made (Michaelis-Menten constant for the sodium-iodide symporter for perchlorate, Km) and the thyroid hormone predictions were adjusted for pregnant mothers and fetuses in the model report under review.

EPA is seeking comments on the scientific rigor of the model for evaluating the effects of perchlorate on thyroid hormones in lactating mothers, breast-fed infants and bottle-fed infants under different iodine intake levels. EPA is providing access to the model program code and all necessary files to facilitate use of the BBDR model by peer reviewers and the public. EPA

expects that those reviewers with the appropriate software and expertise will be able to replicate the results described in the BBDR model report. After completing development of the BBDR model in the acslX software, the U.S. EPA created a copy of the model that can be run in the alternate software, R. The report URL with links to the code (acslX and R versions for both the pregnancy and infant/lactation models) is: [HYPERLINK "https://hero.epa.gov/hero/index.cfm/reference/details/reference_id/3352518"]

Note that the model is calibrated and expected to be valid for conditions where feedback regulation due to variations in thyroid-stimulating hormone (TSH) levels is minimal, so all charge questions regarding the model are for that range.

In March 2016, the Agency invited the public to nominate scientific experts to be considered as panelists for peer review of the draft model and accompanying report. In June, EPA announced that to achieve efficiency it was expanding the scope of the peer review to include draft approaches for application of the model to inform the development of a perchlorate MCLG. EPA has since reevaluated the review process in response to concerns that a simultaneous review of approaches for application of the model to develop a perchlorate MCLG would not allow for prior consideration of peer reviewer comments specifically on the model.

Therefore, EPA seeks public comment and peer review on the modeling approaches and the ability of the model to predict outcomes that could potentially be used to inform the derivation of an MCLG. EPA intends to seek input on the application of the model for developing approaches for a perchlorate MCLG determination at a later date. Future efforts will include discussion of health endpoints and response levels that are most appropriate to base the MCLG determination.

PEER REVIEWERS

Hugh A. Barton, Ph.D.
Pfizer, Inc.

Claude Emond, Ph.D.
University of Montreal

Dale Hattis, Ph.D.
George Perkins Marsh Institute, Clark University

Angela M. Leung, M.D., M.Sc.
UCLA David Geffen School of Medicine

Michael H. Lumpkin, Ph.D., DABT
Center for Toxicology and Environmental Health, LLC.

Elizabeth N. Pearce, M.D., M.Sc.
Boston Medical Center/Boston University School of Medicine

Stephen M. Roberts, Ph.D.
University of Florida

Joanne F. Rovet, Ph.D.
The Hospital for Sick Children (Toronto)

II. CHARGE TO REVIEWERS

1. Model structure: Please comment on the following aspects of the Biologically Based Dose Response (BBDR) model structure and integration of the submodels for iodide/thyroid hormones and perchlorate for each of the life stages of focus (e.g., lactating mother, breast-fed infant, and bottle-fed infant):

    a. Does the developed model structure adequately and accurately describe the physiology and kinetics of iodine, thyroid hormones, and perchlorate during different life stages specified above? Please specifically note the strengths and weaknesses of the model structure for each life stage. Please also suggest approaches to address identified weaknesses in the model structure.

    b. Are the physiological and kinetic parameters for iodine, thyroid hormones, and perchlorate for these life stages supported by the published sources for those parameters or data used to identify parameters via calibration? Please identify any critical data gaps and suggest additional data or parameter (values) to these proposed model parameters to address identified gaps.

    c. While the model predicts the dose-response for fetal thyroid hormones, a reference range for the fetus was not identified. Are there additional data, parameters, or (sub)models available that might be useful for evaluating fetal effects? If not, can the predictions for thyroid hormone changes in the pregnant mother be used as a measure of potential fetal effects?

2. Modifications to existing models: EPA has modified one parameter in the 2013 Lumen et al. model: KM_TPNG, the Michaelis-Menten constant for the sodium-iodide symporter for perchlorate based on Schlosser (2016), and a second key parameter in the 2009 USEPA/2007 Clewell et al. PBPK models: VMAXC_MKP, the maximal velocity for perchlorate transfer to breast milk from those components in the USEPA 2009 models. These two parameters affect perchlorate transport from the mammary plasma to breast milk (VMAXC_MKP) and the strength with which perchlorate inhibits iodine transport by the sodium-iodine symporter (KM_TPNG). Detailed information on the assumptions and data considered in making these changes are provided in the report appendices. Are the changes scientifically supported and reasonably estimated?

3. Model calibration and sensitivity analysis: Please address the strengths and limitations of the model calibration process and the strengths and limitations of the data used for model calibration and evaluation. Identify any additional literature, data, or peer reviewed models that EPA should consider to address identified limitations.

    a. Specifically, is the model calibration and evaluation adequately compared with what is reported in the literature for iodine and perchlorate concentrations in urine, and breast milk and thyroid hormone plasma concentrations under different iodine intake and perchlorate exposure scenarios? Please identify additional studies that would support model calibration that strengthen the proposed model.

b. Are the influential parameters identified in the local sensitivity analysis for total thyroxine (T4) and free thyroxine (fT4) plasma concentrations consistent with known biology? Are there critical data gaps for the influential parameters, which would impact the thyroid hormone predictions? If gaps are identified, please provide approaches that would improve thyroid hormone predictions.

c. Does the proposed model provide the appropriate level of precision and substantiated support for this approach? Please identify any additional limitations of the model's applicability?

4. Hypothyroxinemic reference levels and model predictions: The SAB (2013) recommended that the EPA focus the application of BBDR modeling on the condition of hypothyroxinemia, in which circulating levels of free thyroxine (fT4) are reduced below the normal ("reference") range, but with normal levels of thyroid stimulating hormone (TSH). While the mode of action (MOA) for perchlorate is well described, a defined set of quantitative definitions for reference ranges for hypothyroxinemia during pregnancy or lactation and in infants is not available. For interpretation of the BBDR model, EPA developed a normalization procedure to derive hypothyroxinemia reference intervals and to control for the expected differences between literature results and model predictions.

   a. Please comment on the hypothyroxinemia reference ranges derived for pregnant mothers, fetuses, lactating mothers, breast-fed infants and bottle-fed infants. Is the assumed range between the 2.5^{th} and 10^{th} percentile of the fT4 distribution reasonable? Is it supported by the available data? Has the derivation of the reference ranges, including the normalization process, been appropriately described and supported in the model and the report?

   b. Model predictions for zero intake of perchlorate indicate the range of iodine ingestion for which these life-stages are expected to be euthyroid vs. hypothyroxinemic. Are these predictions reasonable and have they been appropriately described and supported in the model and the report?

   c. Based on the perchlorate level at which each life stage is predicted to become hypothyroxinemic (for a given iodine ingestion rate), it appears that the lactating mother is more sensitive than the breast-fed infant for PND 30-90. In part, this occurs because breast feeding reduces the iodide available for the maternal thyroid. Are these predictions reasonable and have these predictions been appropriately described and supported in the model and the report?

5. Robustness of model predictions and sensitivity at lower perchlorate dose levels: The dose-response predictions from the BBDR model predict levels of fT4 for:
   a) The pregnant mother and fetus at GW40 (Fig. 10);
   b) The formula-fed infant with fixed (Fig. 11, 7 and 30 day infants) and variable (Fig. 12, 7 through 90 day infants) iodine levels in their formula; and
   c) The breast-fed infant as a function of maternal perchlorate exposures and iodine ingestion (Fig. 13, 7 through 90 day infants).

For each of these subgroups, please characterize the extent of uncertainty along the dose-response curve. In particular, is the level of uncertainty acceptable at lower dose levels of perchlorate (e.g., at or below 4 µg/kg/d) and higher levels of iodine intake (e.g., 150 µg/d) for each of these subgroups (left upper corner of the dose-response curves)? Should EPA assume that the model becomes more uncertain with rising perchlorate dose levels and declining iodine ingestion, i.e., as model predictions for fT4 approach and move through the range of hypothyroxinemia. (It should be noted that calibration of the iodide and thyroid hormone sub-models used data for populations with higher iodine intake and background exposure to perchlorate.)

6. Empirical functions to predict thyroid hormone levels: The pregnancy model (but not the lactation/infant models) uses empirical functions to make urinary clearance of iodine and metabolic degradation of T3 dependent on the iodine ingestion level, in order to predict observed nonlinearity in the relationship between thyroid hormone levels and iodine intake. Does this use of empirical functions result in predicted outcomes or trends that are not plausible for serum thyroid hormones, particularly fT4?

7. Characterization of model predictions: The pregnancy and infant/lactation models were developed to specifically consider the range of iodine ingestion and thyroidal uptake where TSH is expected to stay in its normal range (i.e., they do not account for HPT feedback control). Do the models represent a reasonable effort to describe the relationships between iodine intake, perchlorate exposure and thyroid function? Are they sufficiently specific to predict perchlorate-induced changes in thyroid hormones in these life-stages over the range indicated? Please characterize the robustness, precision and sensitivity of the models for the ability to extrapolate changes in T4 associated with perchlorate exposures over the range from low exposures (less than 1 µg/kg/d) to higher levels which the model and analysis predict to be hypothyroxinemic.

References

Clewell RA, Merrill EA, Gearhart JM, Robinson PJ, Sterner TR, Mattie DR, et al. 2007. Perchlorate and radioiodide kinetics across life stages in the human: using PBPK models to predict dosimetry and thyroid inhibition and sensitive subpopulations based on developmental stage. J Toxicol Environ Health A 70:408-428.

Fisher JW, Li S, Crofton K, Zoeller RT, McLanahan ED, Lumen A, et al. 2013. Evaluation of Iodide Deficiency in the Lactating Rat and Pup Using a Biologically Based Dose-Response Model. Toxicol Sci 132:75-86.

Lumen A, Mattie DR, Fisher JW. 2013. Evaluation of Perturbations in Serum Thyroid Hormones During Human Pregnancy Due to Dietary Iodide and Perchlorate Exposure Using a Biologically Based Dose-Response Model. Toxicol Sci 133:320-341.

NRC. 2005. Health Implications of Perchlorate Ingestion. U.S. National Research Council, National Academies Press, Washington, D.C. Available at: [HYPERLINK "https://www.nap.edu/catalog/11202/health-implications-of-perchlorate-ingestion."].

Schlosser P, Leavens T, Ramasamy S. 2016. Biologically Based Dose Response Models for the Effect of Perchlorate on Thyroid Hormones in the Infant, Breast Feeding Mother, Pregnant Mother, and Fetus: Model Development, Revision, and Preliminary Dose-Response Analyses [Public Review Draft]. Other Contributors: Fisher, J.; Lumen, A.; McLanahan, E. Available at: [HYPERLINK "https://www.regulations.gov/document?D=EPA-HQ-OW-2016-0438-0002"].

U.S. EPA. 2009. Inhibition of the sodium-iodide symporter by perchlorate: An evaluation of life stage sensitivity using physiologically based pharmacokinetic (PBPK) modeling. U.S. Environmental Protection Agency, Office of Research and Development, EPA/600/R-08/106A, May 2009. Available at: [HYPERLINK "https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=212508&CFID=80937054&CFTOKEN=35291271"].

U.S. EPA. 2012. White paper: Life stage considerations and interpretation of recent epidemiological evidence to develop a maximum contaminant level goal for perchlorates. U.S. Environmental Protection Agency, Office of Water, Office of Science and Technology, Health and Ecological Criteria Division. Available at: [HYPERLINK "https://yosemite.epa.gov/sab/sabproduct.nsf/0/D3BB75D4297CA4698525794300522ACE/$File/Final+Perchlorate+White+Paper+05.29.12.pdf"].

U.S. EPA. 2013. SAB advice on approaches to derive a maximum contaminant level goal for perchlorate, U.S. Environmental Protection Agency, Science Advisory Board, EPA/ SAB/13/004. Available at: [HYPERLINK "https://www.epa.gov/dwstandardsregulations/perchlorate"].

III. GENERAL IMPRESSIONS

Hugh A. Barton, Ph.D.

Overall this is an extensive systems model that appears to have been carefully and thoroughly developed using available scientific information. The report is generally clear and the logic of the decisions presented seems reasonable. It is difficult to evaluate a model of this complexity by reading the report. This reviewer did not access the model, but in my experience it would take considerable time working with a model of this complexity to develop perspectives on its strengths and limitations.

Claude Emond, Ph.D.

This peer review is part of the U.S. Environmental Protection Agency's (EPA's) National Primary Drinking Water Regulations (NPDWR) initiative for perchlorate a water contamination. This review is also the second phase of Science Advisory Board (SAB) 2013, in which a peer review recommended that EPA should use a physiologically based pharmacokinetic (PBPK) model published earlier, but should integrate the iodine description, including the hormones T3 and T4, to study the hypothyroxinemia and health effects after exposure to perchlorate during lifetime and windows of sensitivity. Two models are presented here 1) mother and fetus PBPK, and 2) mother and infant. Both integrate the previous model of perchlorate that was published and used for the SAB assessment in 2009. These improving versions integrated the iodine/thyroid pharmacokinetic for different stages of life, including the fetus, newborn until 91 days, pregnancy or no pregnancy, and lactation. This report is very well described with transparency and very well referenced for part of the code model, but there is a little fogginess for the m files. The methodology that was used reflects the state-of-the-art employed in pharmacokinetic modeling. I agree that this model is a good start to better understand the mode of action, including the limiting step that we know from literature today. The authors who developed this PBPK model are very knowledgeable in the design of PBPK models; therefore, I am very confident that the design, along with the review that I performed. The combined PBPK model for iodine/perchlorate exposure following sensitive lifetime windows can be used for human risk assessments of health, based on the limitations suggested by the authors. It is interesting to note that the authors also reported a limitation of the PBPK model regarding the range of dose and the windows of sensitivity. I agree with the authors' conclusions regarding the predictability and the limitations of this model. It is important to remember that these models are described for human exposure, which should drastically reduce the uncertainty of the point of departure (POD) used in risk assessment. In addition, the simulations reviewed in this report reproduced relatively well the biomonitoring data published.

Dale Hattis, Ph.D.

Although I have some concerns about the parameterization of the models, my most serious problems with the analysis relate to the choice of population to be modeled and the endpoints that were made the focus of the analysis.

Briefly, in focusing on thyroid hormone changes, the authors have neglected the prime effect of ultimate interest—changes in cognitive development measured as IQ. The latter will need to be a key focus in the mandated "Risk Reduction and Cost Analysis (HRRCA)" referred to in the introduction. IQ differences are readily subject to the comparative economic analysis needed for an HRRCA, whereas it will be difficult to quantify the independent value of thyroid hormone changes themselves for juxtaposition with compliance and other costs of alternative regulatory actions to change exposures. Moreover, studies in the very recent literature, such as those from Holland, provide an excellent basis to quantify effects of both thyroid hormone changes[1] and perchlorate itself[2] during pregnancy on cognitive function as reflected in the IQ measured in the offspring.

Additionally, the focus on modeling of changes in thyroid hormone levels has led the authors to focus their analysis on lactating mothers and breast- and formula-fed infants after birth. This neglects the population groups that are known to be most sensitive to the effects of iodide and thyroid hormone action—women in the first pregnancy trimester, and possibly even the first month of pregnancy before the women may even be aware that they have conceived.[3,4,5]

The Specific Observations on Model Report, at the end of these comments, provides abstracts of recent papers that I think should be used in crafting a better analysis more relevant to EPA's needs in choosing policies to change the existing exposures to perchlorate in the United States.

[1] Korevaar, TIM, Muetzel, R, Medici, M, Chaker, L, Jaddoe, VWB, de Rijke, YB. 2016. Association of maternal thyroid function during early pregnancy with offspring IQ and brain morphology in childhood: a population-based prospective cohort study. The Lancet Diabetes-endocrinology 4:35-43.
[2] Peter N. Taylor, Onyebuchi E. Okosieme, Rhian Murphy, Charlotte Hales, Elisabetta Chiusano, Aldo Maina, Mohamed Joomun, Jonathan P. Bestwick, Peter Smyth, Ruth Paradice, Sue Channon, Lewis E. Braverman, Colin M. Dayan, John H. Lazarus, and Elizabeth N. Pearce. 2014. Maternal Perchlorate Levels in Women With Borderline Thyroid Function During Pregnancy and the Cognitive Development of Their Offspring: Data From the Controlled Antenatal Thyroid Study J Clin Endocrinol Metab 99:4291-4298.
[3] Morreale de Escobar, G, Obregon, MJ, Escobar del Rey, F (2000). Is Neuropsychological Development Related to Maternal Hypothyroidism or to Maternal Hypothyroxinemia? J. Clinical Enocrinology and Metabolism 85: 3975-3987.
[4] Cao, XY, Jiang, XM, Dou, ZH, Rakeman, MA, Ming-Li, Z, O'Donnell, K, Tai, M, Amette, K, DeLong, N, DeLong, R. 1994. Timing of Vulnerability of the Brain to Iodine Deficiency in Endemic Cretinism. New Engl. J. Med 331:1739-44
[5] Bath, SC, Steer, CD, Golding, J, Emmett, P, Rayman, MP. 2013.Effect of Inadequate Iodine Status in UK Pregnant Women on Cognitive Outcomes in their Children: Results from the Avon Longitudinal Study of Parents and Children (ALSPAC)

Angela M. Leung, M.D., M.Sc.

The objective of this proposed BBDR model was to assess the potential adverse thyroidal effects of perchlorate exposure, based on the physiologic kinetics of perchlorate and iodide action on serum free thyroxine (FT4) concentrations among lactating women, their breastfed infants, and

formula-fed infants. Calibration of the model was achieved using published levels of perchlorate and iodine found in breastmilk, maternal urine, and infant urine, and of serum FT4 concentrations in each of these three lifegroups. The model's dose-response relationships between perchlorate exposure and serum FT4 concentrations are reported for various perchlorate exposure and daily dietary iodine intake levels.

The primary endpoint was hypothyroxinemia, defined as the 2.5-10th percentile of serum FT4 concentrations, among lactating women, breastfed infants, and formula-fed infants. Overall, there is less robust evidence in the literature to support the adverse health implications of mildly low serum FT4 concentrations among infants regarding future neurodevelopmental outcomes, compared to the same for pregnant women, in part due to complete reliance of the fetus on adequate maternal iodine and thyroid hormone levels during the first half of pregnancy and the crucial period of rapid neurodevelopment during this time.

The second concern is in regards to the interpretation of published data regarding iodine and perchlorate levels in breastmilk, maternal urine, breastfed infant urine, and formula-fed infant urine; and serum FT4 concentrations in lactating women, breastfed infants, and formula-fed infants. The accuracy of calibration of the model is limited by several issues, including: 1) the use of several relatively small studies containing limited datapoints, particularly for maternal serum thyroid hormone concentrations, 2) the absence of serum thyroid autoantibody data that can influence serum thyroid hormone concentrations, 3) the problems of extrapolation of pregnancy thyroid hormone physiology for the lactation model, 4) the absence of data regarding the timing of dietary iodine intake in relation to breastmilk iodine concentrations in the current available literature, and 5) the inference of analyte and hormone measurement values in the submodels that each assume an exclusive source of infant iodine nutrition.

Finally, the model does not take into account likely coexposures from other environmental and dietary goitrogens, including thiocyanate and nitrate, and it does not consider the dynamics of the hypothalamic-pituitary-thyroid (HPT) axis that is able to respond acutely to even small changes of iodine availability and peripheral thyroid hormone concentrations. Given all of the above and as summarized in much greater detail below, the model presents an estimate of the potential thyroidal effects resulting from perchlorate exposure, but is likely still fairly inexact.

For the record, I am a clinical endocrinologist with research interests in iodine nutrition and environmental thyroid disruptors during pregnancy and lactation, but do not have sufficient background and expertise in modeling to comment on the charge questions that specifically address those aspects of the model.

Michael H. Lumpkin, Ph.D., DABT

The developed model structure adequately captures the known biological processes acting to exchange iodine, TH, and perchlorate across tissue interfaces and transport these molecules across tissue systems and out of the body. The report describes well the representation of the biology in the mathematical model structure. The report describes in detail the selection of data that serve as the basis of model parameter values for the various life stages. This includes the consideration of data published or made available since publication of the foundational BBDR

and PBPK models for perchlorate. Historically, the use of maternal internal dosimetry and pharmacodynamics have been accepted as adequate surrogates for fetal internal doses or effects, are preferable to using maternal administered dose for extrapolation to fetal effects. The justifications for modifying the saturable NIS physiology and NIS transport of iodide and perchlorate into breast milk using more robust data are sufficiently supported in the model report. Given the model structure changes required to align the perchlorate PBPK and iodine BBDR models, the need to revisit the model's fidelity to replicate the Greer et al. data was warranted. The model performance across the various represented life stages appears to be robust for low perchlorate exposures and iodide intake levels resulting in thyroid hormone levels above the 10^{th} percentiles for the reference ranges. Although the model is restricted to represent limited thyroid hormone homeostasis, it represents a plausible and technically justified approach to defining the perchlorate dose-response across a narrow exposure range. An informative analysis would be to further parameterize the NIS transport parameters to adjust the effect of NIS inhibition as T4 levels approach the hypothyroid condition. Using this simple approach, the effect of compensatory upregulation of NIS activity can be explored and evaluated as plausible or not.

Elizabeth N. Pearce, M.D., M.Sc.

The clarity of the writing could be improved; the document is complex and hard to follow. Many of the figures are challenging to interpret: both duplicating information in tables and providing color figures would be helpful. A single glossary including a list of all of the variables as well as the list of abbreviations would be useful for reference.

A more detailed rationale for the choice of hypothyroxinemia as the primary outcome of interest could be provided in the Introduction. This is fundamental for understanding the document which follows.

The literature search, as described on page 22, should be updated with clearly defined search parameters and methodology for study evaluation and selection. It is noted that after 2013 additional papers "later identified as potentially relevant" were added, but there does not appear to have been any formal approach to follow-up literature searches. It would be helpful to broaden the search by considering databases other than PubMed, to institute a systematic framework for study inclusion and exclusion and for evaluating study quality, and to update formal searching. Strategies for these methods have recently been described in an environmental health context (e.g., Morgan RL, Thayer KA, Bero L, et al. GRADE: Assessing the quality of evidence in environmental and occupational health. Environ Int. 2016 Jul-Aug;92-93:611-6). There has been a great deal of new literature since 2013 with relevance to effects of perchlorate on thyroid function and other outcomes in epidemiologic studies; many new pregnancy cohorts in the literature have described thyroid function reference ranges; and there are many new observational studies regarding effects of maternal hypothyroxinemia on child developmental and other outcomes. Some of these new studies could provide support for the selection of hypothyroxinemia as the outcome of interest, and many could provide valuable data for further validating models.

Please note that my expertise is in clinical thyroidology and iodine metabolism. I do not have expertise specifically in the development or use of BBDR modeling. While I comment below on many of the assumptions that went into the models and the data used to validate them, I will need to defer to other peer reviewers with modeling expertise regarding the model code.

Stephen M. Roberts, Ph.D.

It is apparent that a great deal of work has been conducted to develop a proposed BBDR model that is responsive to recommendations by the SAB Perchlorate Advisory Panel. I found the information presented to be accurate, although in some instances incomplete. While the report may serve the purpose of documenting steps taken to create the model, it lacks clarity of presentation in a number of important areas. Problem areas identified include:

1. Confusing presentation. For example, it is not clear from the document whether pregnant women are included in the model described here or are a separate model (modified Lumen et al. model?). Much of the language seems to exclude pregnant women from the model being presented (e.g., "Model development efforts focused on: 1) the lactating mother; and 2) the breast-fed and formula-fed infant for the postnatal period from postnatal day PND) 7 to 90." (pg 6) and "The new BBDR model is intended to predict and evaluate the potential combinatory effects of iodine nutrition and exposure to perchlorate on thyroid function in the infant and lactating mother." (pg 13)) although some modeling results for pregnant women are presented in the report (pg 70). Other examples of sections in the document that are difficult to follow or confusing are included in the responses to charge questions below.

2. Missing explanations/justifications. Although explanations are provided for model inputs, there are important decisions for which no explanation is provided. An example is the decision to model the thyroid hormones in the pregnant woman near term. While normal neurodevelopment requires adequate thyroid hormone throughout gestation, the fetus is particularly sensitive during early gestation. This gives rise to the obvious question of why near term was the time point chosen for modeling. Is it assumed to be representative of earlier gestational time points? Is it, in the opinion of the EPA, in fact the most sensitive time point? Was it simply a matter of the availability of better data for modeling at this time point? Some explanation is needed.

3. Poor graphics. Many of the graphs present multiple plots that are difficult to distinguish.

In addition to describing what is included in the model, it would be useful to also discuss (perhaps in an appendix, companion memo, or some other format), what was not included and why. An example might be a probabilistic treatment of inputs and model output. There can be a number of legitimate reasons why possible inclusions or refinements in the model were not chosen for this iteration of model development, including limitations in time, resources, and/or data availability, or their addition was thought unlikely to significantly improve the model. This is perhaps unusual, but a candid discussion, however brief, would be helpful in understanding the EPA's view why this model, at this time, is considered appropriate.

Joanne F. Rovet, Ph.D.

EPA has requested comments on the scientific rigor of a BBDR model for predicting thyroid hormone perturbations for lactating mothers and breast-fed and bottle-fed infants following their exposure to perchlorate at different levels of dietary iodine intake. This model is an expansion of the one described in a peer-reviewed paper by Lumen et al. (2013) predicting effects for pregnant mothers and fetuses. The current model seeks to address the main recommendations of a Science Advisory Board-Perchlorate Advisory Panel (SAB-PAP) for developing a maximum contaminant level goal or safe perchlorate exposure level for the following sensitive life stages: fetus, pregnant woman, and breast- or formula-fed infant. The PAP group considered these life stages particularly sensitive to perchlorate effects since they reflected stages when the greatest harm from an insufficiency of thyroid hormone would occur to the developing human brain. The pregnant woman was included as a sensitive life stage since she was considered a surrogate for providing thyroid hormone prior to onset of fetal thyroid function when thyroid hormone is critically needed for fetal brain development; the pregnant woman was also considered a supplementary or complimentary source of thyroid hormone in later gestation prior to full function at term.

The current modeling process claims -- for the first time -- to offer a BBDR approach that calculates the adverse consequences of a particular level of perchlorate exposure. Perchlorate is a potent inhibitor of iodide, a key component of thyroid hormone, and is taken up by the maternal, fetal, or infant thyroids or the lactating breast. The model's authors have conceived a reasonable, relatively simple model of biological action and from the literature, have provided an extensive set of realistic parameters and metrics to track the biological actions. These ultimately determine when an infant or lactating mother will become hypothyroxinemic from a specific level of perchlorate in a specific iodine environment. Authors are to be commended for their thorough, systematic, and ambitious approach to capture the situation, particularly on the perchlorate-iodide side of the equation.

However, I have several reservations about the approach and certain assumptions, leading me to sense some naiveté and perhaps lack of understanding on the part of the modelers. First, I am not convinced that the fT4 range used to mark hypothyroxinemia is appropriate and, rather, is too lenient. There is no evidence of what constitutes hypothyroxinemia in an infant and what the exact cut-offs are; these are all based on values from pregnant women. I am also concerned that the thyroid-side of the system may be too simplistic and not correct; the HPT axis, for example, is not modelled. Perchlorate contamination in the water used to prepare formula is not included in the model despite being mentioned in the SAB-PAP (2013) report. The key critical stages set out in the latter, namely pregnant mother and fetus, are for reasons that I do not find convincing disregarded, even though these stages are included in the title and extrapolated in the results; however, I am not sure how this was done. Also, the primary downstream endpoint, namely altered brain development and associated cognitive abilities and behavioral factors, is never considered. The modelling itself is based on old references, which I find concerning in light of the many papers on maternal thyroid dysfunction in pregnancy that have been published in recent years. The process whereby the ultimate 6 papers were selected from the final 62 is not specified. I also would have liked a better description of each of the papers, even if in the Appendix, than the current summary in Table 2. In addition, the model does not account for

other contaminants such as thiocyanate and nitrates that similarly interfere with iodide uptake. The data for the lactating women assume a common start point with regard to iodide sufficiency; however, no attempt is made to examine factors in pregnancy that might also contribute to iodide differences in the breast such as salt intake, particularly iodized salt; dietary factors (kelp, fish, amount of drinking water); use of iodine-containing prenatal vitamins and other supplements; amount of weight gained by mother and size of baby.

Additionally, I was disappointed in the lack of transparency on derivation of results and found the results section, especially the figures, which are relatively poor quality, hard to interpret. The latter aspect is particularly disheartening given the beautiful graphics supplied by "R". To improve clarity, all figures also would have benefited significantly by better more extensive figure captions. Overall, I found the Results section very poorly organized and hard to follow, very preliminary and rushed, almost as a first draft. It was not clear to me how data on pregnancy and fetal development were derived. While somehow, I think this is extrapolated back to birth at 40 weeks' gestation, to me this does not adequately represent the period of pregnancy nor fetal life. The writing generally carried a degree of vagueness (e.g., "adequate" p. 60; "within the range" p. 62) and lack of precision and it was generally quite difficult to follow the information in the figures from the corresponding text. Finally, as there was no proper ending to the report and no conclusions or take-home message, I was left with a sense of confusion – and disappointment. This was especially apparent in the Local Sensitivity Analysis that lacked proper discussion. This report should be readily understandable by persons of all disciplines; I sense it is written mostly for modelers and sometimes in modelling lingo.

IV. RESPONSE TO CHARGE QUESTIONS

Question 1. Model structure: Please comment on the following aspects of the Biologically Based Dose Response (BBDR) model structure and integration of the submodels for iodide/thyroid hormones and perchlorate for each of the life stages of focus (e.g., lactating mother, breast-fed infant, and bottle-fed infant):

Question 1A. Does the developed model structure adequately and accurately describe the physiology and kinetics of iodine, thyroid hormones, and perchlorate during different life stages specified above? Please specifically note the strengths and weaknesses of the model structure for each life stage. Please also suggest approaches to address identified weaknesses in the model structure.

Hugh A. Barton, Ph.D.

This question really requires expertise in thyroid hormone, iodine, and perchlorate biology. As an expert in modeling I cannot directly comment on how well the model structure captures the biology.

One question raised in the public comments was whether there were regulatory processes that would occur at low iodine and T4 levels, such as induction of NIS. It would be good to know whether there is information on this point.

Another question raised in public comments about the model structure was the change from a three compartment thyroid to a two compartment description. From the text on p 30, it appears that having a consistent structure in the fetal (Lumen et al., 2013) and the infant models might have been part of the rationale for this change. This could be clarified and perhaps some information provided as to the value provided by the three compartment description in previous modeling by comparison with this two compartment approach; was this a model simplification that had relatively modest impacts on model behaviors or was this a more substantial change or is this not known?

Claude Emond, Ph.D.

Strengths:

- The way in which the authors describe the codes in acslX in the 2 models was relatively easy to follow and well referenced for the CSL file.
- Comparing the simulation to the biomonitoring data from the literature, we can say that the predictability of the model is acceptable.
- The confidence in the models should be qualified by a medium that is inside the limitation of the model.

Weaknesses:

- The conceptual PBPK model structure (Figure 3) does not describe what the codes represent. The model codes describe kidney, liver, mammary

gland, GI_{tract}, skin, and thyroid and so on. It should be easier to incorporate these compartments inside of Figure 3.

- The way the codes are described, it seems that there is interlace between several models in unique code files. This can be a problem if some users are inexperienced; therefore, users of the model must have previous experience with models in order to use the combined version.
- It would be also interesting in the future to incorporate mother, fetus, lactation and infant in the same model.
- Even the 'csl' files are good, it is more tricked for the ''.m'' files. For me this part missed the objective of transparency. The 'm' files can reproduce the graph cited in the report, but it is difficult to understand the logic simulation behind them. It will be important for the upcoming user to understand the mechanics behind the result.
- If I have not missing something, it seems that the fetus model has a fixed constant (3.4 kg) for body weight. It does not consider all the fetus formation, but only the week 40. Is there a rational behind this or is it due to a lack of data?

Dale Hattis, Ph.D.

As indicated above, I disagree with the focus on the specific life stages chosen for detailed analysis. If the shift is made to quantifying cognitive impairment rather than just thyroid hormone level changes, as I recommend, I think it would be much better to model fetal and maternal perchlorate effects on perchlorate and thyroid hormone levels in early pregnancy.

There are no obvious problems with the model structures used to describe these kinetics.

Angela M. Leung, M.D., M.Sc.

Comments regarding physiology and kinetics of the model structure:

The focus of the overall model is the potential adverse effect of perchlorate exposure in the lactating mother and in the infant (both breastfed and formula-fed) during ages days 7-90 of postnatal life. The model considers the kinetics of and physiology between perchlorate exposure, dietary iodine nutrition, and serum thyroid hormone concentrations in the lactating mother, breastfed infant, and formula-fed infant. The primary endpoint is hypothroxinemia, defined as the 2.5-10^{th} percentile of serum FT4 concentrations among lactating women, breastfed infants, and formula-fed infants. Some general comments are as follows:

- It would be reasonable to consider the full HPT axis, given the interdependence of serum TSH and FT4 concentrations on the changing effects of iodine nutrition and perchlorate exposure. The assessment of serum FT4 concentrations in isolation is a limitation of the physiologic responses that occur with dynamic variations of iodine supply, as incurred with constantly changing dietary intake, breastfeeding, and urinary excretion.

- The role of coexposures by other environmental toxicants, such as thiocyanate and nitrate, should be assessed in reference to the effects of perchlorate during these life stages. The potency of perchlorate, relative to thiocyanate and nitrate, as a competitive inhibitor of iodine at NIS should be considered.
- The longterm concern of perchlorate exposure during crucial periods of early development is on the possible detrimental neurocognitive effects among exposed fetuses and infants. The current literature surrounding the associations of maternal hypothyroidism and/or hypothyroxinemia on later offspring neurodevelopment is generally better-established than that for infant hypothyroxinemia.

Regarding the applicability of the model for each of these three life stages:

a. **Lactating mother**: Perchlorate exposure in the lactating woman is assumed to be from ingestion through the diet. The present model reflects an integration of the previous PBPK perchlorate models predicting thyroidal RAIU inhibition with the PBPK iodine and BBDR thyroid hormone models, which were based on the previously published pregnancy model. For the analyses, maternal iodine intakes are assumed to range between 75-250 mcg/day, and maternal perchlorate exposures up to 20 mcg/kg/day are assessed. For reference, major points reviewed are:

- The previous *pregnancy* model (page 18, lines 1-13) assumed dietary iodine intakes of >200 mcg/day, but notes that model dose-response predictions for iodine intakes ≥150 mcg/day are judged to be similarly reliable, given the very small decrease in serum FT4 concentrations between the two levels. The pregnant mother also was predicted to have a lower baseline serum FT4 concentration (in the absence of perchlorate) than the lactating mother at postnatal day 7, given the same amount of dietary iodine.
- The *lactating* model (page 18, lines 20-25) assumes dietary iodine intakes of >250 mcg/day, but notes that model dose-response predictions for iodine intakes ≥150 mcg/day are judged to be similarly reliable, given the very small (6-14%) decrease in serum FT4 concentrations between the two models. At postnatal days 7-90, the lactating mother's serum FT4 concentrations are predicted to decrease due to the physiological changes and demands of breastfeeding.
- At postnatal day 7 for the lactating mother, the steepness of the perchlorate dose-response for maternal serum FT4 concentrations is similar to that for the pregnant mother. The model predicts that if maternal perchlorate exposure is <4 mcg/kg/day, both the pregnant and lactating mother maintain normal serum FT4 concentrations if their dietary iodine intakes are at least >150 mcg/day.
- Sensitivity analyses suggest that maternal parameters impacting breastmilk iodine concentrations, amount of breastmilk ingestion, and kinetics of thyroid hormone physiology and urinary excretion of iodine are important predictors of serum FT4 and TT4 concentrations in the breastfed infant.
- The maternal sub-model as shown in Figure 3 was reviewed in detail for this question.
    - **Strengths**:

1-- The model considers available published data regarding iodine, perchlorate, and serum FT4 physiology and concentrations during pregnancy, lactation, and early infancy, though with several important caveats.

2-- With the exception of the comments below, the maternal sub-model addresses the kinetics of iodine and thyroid hormone physiology during lactation.

- **Weaknesses**:

1-- Maternal urinary iodine levels are not accounted for in the maternal sub-model as shown in Figure 3. There are data reporting that estimated urinary iodine 24-hour excretion in the mother, rather than spot maternal urine iodine concentrations, are a good reflection of maternal iodine supply to the breastfed infant (Andersen SL et al; PMID 2419933); these data also demonstrate that breastmilk iodine concentrations are not correlated with maternal fluid intake.
2-- Also not shown in Figure 3 is the active transport and concentration of perchlorate into mammary cells during lactation by NIS (Dohan O et al; PMID 18077370), which is significant for the potential of perchlorate exposure from breastmilk to directly inhibit the infant's thyroidal iodine uptake.
3-- The relative potency of perchlorate as a competitive inhibitor of iodine uptake at NIS (30:1 affinity to iodine) should be included (Tonacchera et al; PMID 15650353).

b. **Breastfed infant**: Perchlorate exposure in the breastfed infant is assumed to be from breastmilk ingestion and focuses on the effects of exposure during postnatal days 7-90. For reference, major points reviewed are:

- At postnatal day 7, the perchlorate threshold associated with breastfed infant serum FT4 concentrations decreasing to below the lower limit of the reference range is 12 mcg/kg/day.
- During postnatal days 7-90, the model predicts that maternal perchlorate exposure reduces breastfed infants' serum FT4 concentrations, with the magnitude of decrease inversely dependent on maternal dietary iodine intake.
- During postnatal days 30-60, breastfed infants' serum FT4 concentrations would be predicted to remain within the reference range when maternal dietary iodine intakes are ≥150 mcg/day and maternal perchlorate exposure is <20 mcg/kg/day, even though maternal thyroid function is expected to be abnormal (hypothyroxinemic or hypothyroid) in these ranges.
- Overall, the model predicts a larger effect on serum FT4 concentrations in breastfed infants than formula-fed infants, due primarily to the higher perchlorate concentrations in breastmilk than infant formula in general; this discrepancy is then further exacerbated when breastmilk iodine content is low from insufficient maternal dietary iodine intake.
- The infant sub-model as shown in Figure 2 was reviewed in detail for this question.

- **Strengths:**

1-- The model considers data from the existing literature regarding iodine, perchlorate, and serum FT4 physiology and concentrations during lactation for the breastfed infant.

- **Weaknesses:**

1-- Similar to the comment above regarding the lactation mother, what is not shown in Figure 2 is the active transport and concentration of perchlorate into mammary cells during lactation (Dohan O et al; PMID 18077370), which is significant for the potential of perchlorate exposure from breastmilk to directly inhibit the infant's thyroidal iodine uptake.

2-- Perchlorate inhibition (as shown in yellow in Figure 2) might be better clarified if the potential sources of perchlorate exposure in the breastfed infant were also shown (i.e., breastmilk, formula), similar to what is shown for sources of iodine.
3-- One major limitation is the significant variability of breastmilk iodine concentrations in the existing literature upon which the model is built. Please see my comments in Question 1B regarding this.
4-- The recommendations for dietary iodine intake in infants should be referenced. The U.S. Institute of Medicine estimates that the Adequate Intake for infants ages 0-6 months is 110 mcg iodine/day. This is based on iodine turnover studies showing that iodine requirements in term infants is 15 mcg/kg/day (Comprehensive Handbook of Iodine, 2009).

c. **Formula-fed infant**: Perchlorate exposure in the formula-fed infant is assumed to be from infant formula ingestion and focuses on the effects of exposure during postnatal days 7-90. For reference, major points reviewed are:
- For all postnatal days and infant formula iodine concentrations studied (108-384 mcg/L), the model predicts infant serum FT4 concentrations to stay within the reference range.
- Perchlorate exposure from infant formula would be expected to reduce infant serum FT4 concentrations at postnatal day 7, but not between postnatal days 30-90, for all infant formula concentrations.
- The infant sub-model as shown in Figure 2 was reviewed in detail for this question.

- **Strengths:**

1-- The model considers data from the existing literature regarding iodine, perchlorate, and serum FT4 physiology and concentrations during lactation for the formula-fed infant.
2-- The infant model was developed on the assumption that the iodine content of infant formulas ranges from approximately 100-300 mcg/L. Thus, for the described kinetics of infant formula intake, these infant formula iodine concentrations are predicted to be sufficient for normal thyroid hormone production in the formula-fed infant (page 18, lines 14-17).

- **Weaknesses:**

1-- The infant sub-model as shown in Figure 2 does not show the potential of perchlorate exposure that can also occur from infant formula ingestion (Pearce EN et al; PMID 17311853).
2-- Perchlorate inhibition (as shown in yellow in Figure 2) might be better clarified if this potential source of perchlorate exposure in the formula-fed infant was also shown, similar to the what is shown for sources of iodine.
3-- The recommendations for dietary iodine intake in infants should be referenced. The U.S. Institute of Medicine estimates that the Adequate Intake (an estimation of the Recommended Daily Allowance [RDA] when there are insufficient data) for infants ages 0-6 months is 110 mcg iodine/day. This is based on iodine turnover studies showing that the iodine requirement in term infants is 15 mcg/kg/day (Comprehensive Handbook of Iodine, 2009).

Michael H. Lumpkin, Ph.D., DABT

The developed model structure adequately captures the known biological processes acting to exchange iodine, TH, and perchlorate across tissue interfaces and transport these molecules across tissue systems and out of the body. The report describes well the representation of the biology in the mathematical model structure. A possible weakness in the model is the lack of TSH expression, and the assumption that TSH expression discretely activates in a population *in*

situ at the 2.5th percentile of plasma T4/fT4. While there may not be adequate data at this time to value-populate a parameter for TSH-induced up-regulation of NIS in the thyroid or mammary gland, the addition of such a parameter followed by a local sensitivity analysis of up-downregulation of NIS would be informative to explore wither chronic perchlorate exposure and low-level TSH expression would likely or not affect plasma and breastmilk T4 levels at all life stages.

Elizabeth N. Pearce, M.D., M.Sc.

Although the choice of hypothyroxinemia as the primary outcome of interest was previously established by the SAB, the strengths and weaknesses of this approach at each life stage deserve consideration.

Strengths of this approach include efforts to identify both the particularly vulnerable life stages and the most significant public health outcomes which are potentially associated with perchlorate exposure. In thinking about the potential public health impact of perchlorate exposure, potential adverse outcomes essentially overlap those of iodine deficiency, and the potential adverse effects on fetal and child neurodevelopment are of paramount interest. There are relatively few data at present to support an effect of maternal subclinical hypothyroidism on lowered child IQ (a study by Haddow et al. included both overtly and subclinically hypothyroid women: Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, O'Heir CE, Mitchell ML, Hermos RJ, Waisbren SE, Faix JD, Klein RZ 1999 Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med 341:549–555). However, there is a growing body of evidence demonstrating adverse child developmental effects of maternal hypothyroxinemia in pregnancy (in addition to those cited in the report, see papers listed below under 3A). Importantly, these studies have assessed maternal free T4 in early to mid-gestation; links with third-trimester maternal hypothyroxinemia have not been established.

There are some limitations regarding the choice of hypothyroxinemia at certain life stages as the primary outcome of interest. Despite the observational data suggesting a link between early gestational maternal hypothyroxinemia and adverse child developmental outcomes, there are now two randomized clinical trials (Lazarus JH, Bestwick JP, Channon S, Paradice R, Maina A, Rees R, Chiusano E, John R, Guaraldo V, George LM, Perona M, Dall'Amico D, Parkes AB, Joomun M, Wald NJ 2012 Antenatal thyroid screening and childhood cognitive function. N Engl J Med 366(6):493-501 and [HYPERLINK "http://www.ajog.org/article/S0002-9378(15)01319-8/pdf"]) which demonstrate no benefit of levothyroxine treatment for maternal hypothyroxinemia on child IQ. (It is worth noting that both of these trials were limited by relatively late initiation of therapy; at 13 weeks in CATS and at 17 weeks gestation in the Casey study.) Given both the lack of interventional data demonstrating treatment benefit, and the challenges of establishing maternal free T4 reference ranges and treatment targets, current clinical guidelines (including in-press updated guidelines from the American Thyroid Association) largely recommend against levothyroxine treatment for isolated maternal hypothyroxinemia. In addition, in lactation, maternal hypothyroxinemia has not been defined as a clinical syndrome and has not been linked to any adverse outcomes. Therefore, normative reference ranges for thyroid function tests specifically in lactation have not been established.

Infant hypothyroxinemia might lead to impaired neurodevelopment, but data for normal free T4 ranges in infants are limited.

The lack of consideration of the HPT axis in the BBDR model is a very substantial limitation of the model at each life stage. Clinically it is virtually never appropriate to interpret free T4 in isolation, without consideration of the serum TSH and other thyroid function test values. Decreases in thyroid hormone stimulate increases in TSH; higher TSH levels, in turn, will increase the affinity of the thyroid for iodine uptake, increase the ratio of T3 to T4 synthesized by the thyroid (which may have important implications for the fetus, given that transplacental passage of maternal thyroid hormone is primarily of T4, not T3), and cause thyroid hyperplasia. There is also a good deal of interpersonal variation in compensatory mechanisms, so that I am not sure it is fair to state (as on page 69) that hypothyroidism is expected when the free T4 drops to the 2.5th percentile.

It is notable that environmental exposures to perchlorate do not occur in isolation; exposure to thiocyanate and nitrate is equally ubiquitous and works by the same mechanism of NIS inhibition. It, therefore, would seem pertinent to include variable co-exposure to thiocyanate and nitrate in the models. Given available data in the literature about exposures at different life stages and about the relative effects on NIS inhibition, this addition would likely not be terribly difficult.

Excessive, as well as inadequate iodine exposure is associated with adverse effects on thyroid function; models do not appear to account for potential non-linear effects of iodine exposure on thyroid hormone status. This is likely not of concern at the range of iodine intakes being studied, but this could at least be considered.

Stephen M. Roberts, Ph.D.

When the SAB Perchlorate Advisory Panel recommended a novel approach for perchlorate MCLG development, it envisioned a framework with which the complexities of a perchlorate MOA could be addressed using a PB/PK-PD approach, extending from perchlorate exposure through NIS inhibition to thyroid hormone changes and finally to neurodevelopmental impacts. While some useful modeling had already been done, it was recognized that building out all of the PK and PD aspects could take considerable time and resources, as well as new research. In view of practicalities, including the need to develop a new perchlorate MCLG in a timely manner, some interim steps were suggested that could lead to a scientifically defensible MCLG that could be updated as the model is refined in the future. A strength of the BBDR model structure proposed here is that it includes all of the essential elements: perchlorate and iodine PK, NIS inhibition, and thyroid hormone changes associated with neurodevelopmental effects. It addresses all of the sensitive life stages identified by the SAB panel.

There are pieces that are missing — limitations may be a better term than weaknesses. One is the influence of co-exposure to other goitrogens and another is the inclusion of more explicit quantitative relationships between thyroid hormone disturbances and neurodevelopmental outcomes. Both were noted by the SAB panel as desirable to include, but were considered to be elements that could only be added in a meaningful way after additional research.

Given the information that is available now with which to construct a PB/PK-PD (BBDR) model, I have no problems with the overall model structure presented, and accept the explanations for simplification of some of aspects of the model from previous versions (i.e., reduction in thyroid subcompartments and direct transfer of iodide from mammary plasma to milk). Within the constraints of the model, its ability to "adequately and accurately describe the physiology and kinetics of iodine, thyroid hormones, and perchlorate during different life stages" is a function largely of the values chosen for the various parameters rather than the model structure itself.

Joanne F. Rovet, Ph.D.

As above, the model appears to be stronger regarding kinetics of iodide and effects of perchlorate on iodide synthesis than in specifying thyroid-hormone actions and making predictions from the latter set of specifications. The HP-part of the HPT axis is not included nor is the role of deoidinases. The assumption that fT4 is converted equally to fT3 and RT3 is in my belief not correct, even though accepted in the Lumen et al (2013) model. It is well established that within the brain, T4 is the primary hormone of action. T4 enters the brain via the glia, where it is locally to T3 by the D2 enzyme. These pathways are not currently considered. Additionally, free T4 is considered the key hormone but isn't bound hormone (as measured by total T4) the hormone that gains entry into the brain at the blood-brain barrier or choroid plexus? Finally, the assumption that the P7 infant is equivalent to the neonate is wrong given Vulsma's data showing a steep drop-off in levels of T4 following birth in children with congenital hypothyroidism, thought to reflect the loss of the maternal contribution following parturition. To my knowledge, no evidence exists showing the infant thyroid gains this capacity in the first week of life.

The breast-feeding infant model combined with the lactating mother is to me a single system that is well thought out in showing points of impact of perchlorate, whereas the bottle-feeding infant model fails to realize the impact of perchlorate in the water used to prepare formulas after the infant has graduated from premade formulas (at about 1 month of age). A greater risk of hypothyroxinemia in the lactating than bottle-feeding mother is not known and it is not clear to me why this would represent a sensitive stage when the real issue is the developing brain and its high need for thyroid hormone. Perhaps authors were considering the relationship between hypothyroxinemia and maternal depression in the post-partum period. However, to my knowledge, the only person to study this is Victor Pop who examined prenatal, not postnatal, hypothyroxinemia and this would be equally present in both types of mothers (i.e., those who do and those who do not breast feed).

Question 1B. Are the physiological and kinetic parameters for iodine, thyroid hormones, and perchlorate for these life stages supported by the published sources for those parameters or data used to identify parameters via calibration? Please identify any critical data gaps and suggest additional data or parameter (values) to these proposed model parameters to address identified gaps.

Hugh A. Barton, Ph.D.

The basis for the model parameters is provided in Tables 4 – 8. In general, it appears the parameters are supported by some information (sometimes visually fitted to the data or the data used directly as table functions).

As also noted in public comments, when the basis of a parameter value is provided as a previous modeling effort (e.g., Fisher et al 2016, Lumen et al 2013), this is a secondary source that does not directly identify the supporting information. In several cases additional information is provided, for example the original data source used for the previous modeling. Ideally, this approach would be used for all instances where other models are noted.

In addition, as also noted in public comments, the report states on p 23 that "The review process was halted after it was judged that the objective had been met; i.e., sufficient data for model calibration had been identified." It is not clear what the statement means or how it was decided there were sufficient data. It is also not clear if this means the review of papers from the Dec 2013 search was halted or that further searches of literature were halted. Finally, given the time required to develop the model and prepare documentation, context should be provided for the Dec 2013 date, e.g., initiation of this model development effort, so it does not appear to be several years out of date for no reason. While it will likely never be possible for the model to catch up with the most current publications, it might be reasonable to carry out searches to determine what new publications were available and whether they essentially augmented existing information (e.g., another cohort of pregnant women with similar measures as previously existed) or potentially provide new information about parameters with assumed values.

Claude Emond, Ph.D.

The physiological parameters are clearly and transparently presented in both model CSL files. When no data were present in the literature to establish the biological relevant, the authors optimized the parameters to fit the biomonitoring human data published. The review draft is very well referenced and helps to build our confidence in using the model.

Dale Hattis, Ph.D.

Briefly, I find several of the comparisons between observations and model predictions unconvincing. For urinary iodide the key discussion appears on page 60:

*"First, model predictions of urinary iodide concentrations for the formula-fed infant were compared with data from Gordon et al. (2014) and Cao et al. (2010). The model simulations were performed based on formula concentrations of iodine reported by Pearce et al. (2004) and perchlorate by Schier et al. (2010). Urinary iodide predictions were not sensitive to perchlorate exposure levels, so for these simulations, the geometric mean perchlorate concentration (0.92 14 µg/L) of all formulas analyzed by Schier et al. (2010) was used for the iodide comparisons (**Figure 4**, top panel). The model-predicted urinary iodide concentration for formula-fed infants with iodine concentrations at the lowest reported value of 108 µg/L by Pearce et al. (2004) were within the range of literature-reported values (**Figure 4**) from Gordon et al. (2014) and from Cao et al. (2010) for both cow milk-based and soy-based formula."*

The figure referred to has an enormous amount of scatter, even with the data points plotted on a logarithmic y-axis. To then say, given this scatter, that "the model-predicted urinary iodide concentrations…were within the range of literature-reported values (Figure 4) really is such a loose standard that it seems hardly meaningful. Minimally there needs to be some statistical summarization of the comparison data and some specific comparison of the summary data with specific sets of model predictions from models incorporating a range of possible values of key parameters.

The perchlorate comparison is discussed on page 61:

*For perchlorate, data for urinary concentrations were only available for formula-fed infants from Cao et al. (2010). To cover the range of literature-reported perchlorate concentrations, simulations are shown for 0.18 µg/L (minimum measured by Schier et al. (2010)), 0.92 µg/L (geometric mean of values for both soy and cow milk formulas from Schier et al. (2010)), and 4.1 µg/L (maximum value from Pearce et al. (2004), which is higher than the maximum measured by Schier et al. (2010)). Model-predicted concentrations of perchlorate were within the reported values for cow and soy formulas (**Figure 4**, bottom panel)*

The comparison depicted in the bottom panel is also unconvincing, lacking any statistical summarization to help the reader judge whether the comparison supports or refutes the predictions of the model.

Further discussion of the comparison of perchlorate levels appears on page 63:

*The model-predicted urinary perchlorate concentrations were within the range of reported values for birth to 90 days for both formula-fed and breast-fed infants, when perchlorate daily intake was assumed to vary between 0.001 and 1 µg/kg/d (**Figure 6**; data from Leung et al. (2012) and Cao et al. (2010)). Since iodine intake between 75 and 250 µg/day had no effect on predicted urinary perchlorate levels, the iodine intake by the lactating mother was assumed to be 150 µg/day for the perchlorate comparison: a low level within the plausible range for which the model is assumed valid. Since iodine intake has very little effect on predicted perchlorate kinetics, the exact choice of iodine level is not important for this comparison.*

Similarly the conclusion from Figure 6 that the predicted perchlorate concentrations are "within the range of reported values" is completely unconvincing. What is shown in Figure 6 is a plot of

highly scattered observations plotted over a four order of magnitude range with no statistical summarization of the data to allow reasonable juxtaposition of the central tendency and uncertainty range of the observations with corresponding model expectations.

There is a discussion of a comparison of iodide levels on page 64:

*Note: it has been suggested that iodide levels are not stable in breast-milk samples (Dr. Benjamin Blount, CDC, personal communication), which may explain in part why many of the data in **Figure 7** (also see **Figure 17**) are well below the model simulations for 150 and 250 µg/d maternal iodine intake. The predictions for the lowest iodine intake of 75 ug/d are closer to the middle of the range of the data.*

The lack of correspondence of the data points to model predictions is unsettling. And the proffered explanation "that iodide levels are not stable in breast-milk samples" is no help. Instability would be expected to lead to scatter of the data points, but not a systematic bias lowering the data points relative to model expectations. The modelers' response in this case makes no sense.

The overall conclusion of the authors appears on page 67:

*Overall, the model predictions were considered adequate based on the comparison of model 11 simulations to data in **Figure 4-Figure 9***

I disagree. The authors should develop a range of alternative models that would fit these data as well or better based on much more rigorous criteria than that the models produce results "within the range" of the observations presented on multi-order-of magnitude plots. They should then consider and document range of policy-relevant parameter values indicated by running the alternative models with the range of plausible calibrations.

Angela M. Leung, M.D., M.Sc.

Comments regarding calibration parameters:

The models consider published literature to support the calibration parameters for iodine, thyroid hormones, and perchlorate in the lactating mother, breastfed infant, and formula-fed infant.

a. **Lactating mother calibration parameters:**
   - **Iodine in the lactating mother**:
     - Variability of breastmilk iodine concentrations: The parameters for breastmilk iodine concentrations are based on mean values drawn from women examined in relatively small studies. One potentially substantial limitation is that data demonstrating a significant variation of breastmilk iodine concentrations following the ingestion of dietary iodine (Leung et al; PMID 23050787) was not included in the model. In this study of 16 healthy euthyroid lactating women, dietary iodine consumption (600 mcg oral KI) following an overnight fast increased breastmilk iodine

concentrations by nearly 8-fold within a few hours, thus illustrating the limitations in the interpretation of random breastmilk iodine content measurements and the challenges of basing the model on mean breastmilk iodine values from relatively small studies. This is hinted at on page 40 lines 5-10 and also on page 6/Figure 6. From the data of Leung et al. (PMID 23050787), the statement on page 40 lines 8-10 is thus inaccurate. Given the impossibility of ascertaining the influence of recent dietary iodine intake in relation to breastmilk iodine values reported in the literature, one can perhaps assume that the lowest and highest range of reported breastmilk iodine values may be that representing all scenarios of dietary iodine intake; this is important to note in the model report as a limitation and caveat to the model. Incidentally, the median (IQR) *fasting* breastmilk iodine concentration in this study was 45.5 mcg/L (34.5-169 mcg/L), which is comparable to the Leung 2012 study used for calibration of the current model.

- Mean breastmilk iodine concentrations: Recognizing that in the absence of a larger study assessing the impact of dietary iodine on breastmilk iodine concentrations, the model can only rely on mean breastmilk iodine concentrations taken from random collections as much as possible. Other U.S. data on breastmilk iodine concentrations have been reported in 57 healthy women (Pearce et al; PMID 17311853) that are not included and can be used to improve the calibration of the model. This study by Pearce et al also reports the perchlorate content in the subjects' breastmilk; urinary iodine and perchlorate concentrations; and 17 brands of infant formula that subjects reported use of during pregnancy.
- Breastfeeding exclusivity: An important caveat is that many of the studies in the literature did not examine women who were exclusively breastfeeding, and thus the iodine nutrition provided to their infants was derived from a combination of breastmilk and formula sources. Calibration of the model to the published ranges of iodine and concentrations in breastmilk, maternal urine, and infant urine, and for infant serum thyroid hormones may thus be inaccurate.

- **Thyroid hormones in the lactating mother:**
  - TT4 reference range:

1. The *pregnancy* model is based on TT4 reference ranges as reported in 6 studies (page 20, lines 5-7). The *lactation* model is based on serum FT4 concentrations from only 48 total women from two NHANES cohorts (page 20, lines 16-22). The small n used for the lactation model is concerning for its accuracy. Also, it should be stated clearly in the text that the following influence serum thyroid hormone concentrations during pregnancy and lactation: preexisting thyroid disease and/or use of thyroid hormone replacement or antithyroidal medications, positive serum thyroid autoantibodies, hyperemesis gravidarum, trophoblastic disease, and preeclampsia, and whether these were assessed in any of the quoted studies from which the models are based.

2. There are several potential concerns regarding the adaptation of the human pregnancy thyroid physiology model for use in the lactation model. In general, thyroid hormone requirements are increased in pregnancy, compared to lactation, due to the following factors: 1) It is well-known that thyroid hormone requirements and thus, thyroid hormone production, increases by approximately 2-fold from the beginning of pregnancy to mid-gestation, due primarily to the increases in thyroid binding globulin (TBG) that is seen with increased estrogen levels during pregnancy (Glinoer; PMID 9183570). The thyroid hormone requirements decrease back to pre-pregnancy levels following delivery. 2) There are rises in serum FT4 concentrations, particularly during the first trimester, due to the rise of beta-HCG during this timeframe. 3) There is an increase in plasma volume during pregnancy that corresponds to increased thyroid hormone requirements during pregnancy. 4) There is an acceleration of serum T3 and T4 degradation during pregnancy, due to the effect of abundant type 3 deiodinase expression and activity in the placenta and uterine and fetal tissues. In summary, for these reasons, the extrapolation of serum thyroid hormone levels during pregnancy for use in lactation is not ideal (page 14 lines 11-12). For the lactation model, non-pregnant serum thyroid hormone concentrations would be more accurate.

- **Perchlorate in the lactating mother:**
  - The report states that the details of the EPA perchlorate and radioiodide PBPK models for the lactating mother are referenced in McLanahan et al 2014 and U.S. EPA 2009. The current model was simplified from the previous PBPK models according to the following changes: the thyroidal subcompartments for perchlorate was reduced to plasma and tissue (similar to iodine), and perchlorate transport in mammary cells is shown to occur as a one-step process from plasma to breastmilk. Key perchlorate PBPK model parameter changes resulting from these revisions are summarized on pages 44-45 of the report. My expertise is not in this area, and I am unable to comment further regarding this question.

b. <u>Breastfed infant calibration parameters</u>:

- **Iodine, thyroid hormones, and perchlorate in the breastfed infant**:
  - <u>Leung et al 2012 publication</u>: It should be noted that the report by Leung et al 2012 used in calibration of the model included both exclusively breastfed infants (35% of the sample size), as well as those who also partially consumed infant formula (65% of the sample size). This clarification is missing from Table 2 and in the corresponding text; it is a significant limitation of the current model, as it assumes that all data was obtained from exclusively breastfed infants.
  - <u>Cao et al 2010 publication</u>: Similarly, this report included both breastfed infants (46% of the sample size) and formula-fed infants (54% of the sample size), as noted in Table 2. The use of urinary iodine and perchlorate concentrations from this study for model calibration thus is not completely accurate when assuming they are resulting from exclusive breastfeeding or exclusive formula-feeding.

- Colostrum iodine concentrations: The report outlines the reasons for not analyzing neonates between days 0-7 of postnatal life, primarily the physiologic surge of TSH levels in the immediate postpartum period, which is a valid argument. However, there are data examining perchlorate and iodine levels in colostrum (form of breastmilk beginning in late pregnancy and continuing in the first few days after delivery) and in the urine of postpartum women (Leung et al; PMID: 18616704). These data may be helpful to include in the report to further strengthen the current model's relationships between perchlorate exposure and breastmilk iodine levels in lactating women; the relationship does not have to be included in the model, but can be used to assess trends of the impact of perchlorate exposure when comparing neonates <7 days to those >7 days of newborn life. A study has reported that the estimated iodine intake from breastmilk and infant formula during this early period, days 1-2 after birth, are 20.0 ± 11.9 mcg/day and 13.0 ± 3.3 mcg/day, respectively (Gokmen IG et al; PMID 7661341).
- Maternal 24-hour urinary iodine excretion: There are data reporting that estimated urinary iodine 24-hour excretion rates in the mother are a better reflection of iodine supply than perhaps breastmilk iodine to the breastfed infant (Andersen SL et al; PMID 2419933) for the reasons delineated in response #1Ba (*calibration parameters for breastmilk iodine in the lactating mother*). It is interesting to note that these data by Andersen et al also demonstrate that breastmilk iodine concentrations are not correlated with maternal fluid intake.

c. **Formula-fed infant calibration parameters:**

- **Iodine in the formula-fed infant**: The model is built on data by Pearce et al 2004 that reported the iodine content of eight brands of U.S. infant formula. Given this limited data, it may be worthwhile to also consider additional available data:
  - There is an additional study of U.S. brands of infant formula reporting a detectable range of perchlorate in all 17 products tested (range, 0.22-4.1 mcg/L) (Pearce EN et al; PMID 17311853).
    - Although it is a Spanish study, the measured iodine content of 27 brands of infant formula in Spain (Fernandez-Sanchez LM et al; PMID 18039487) report a mean iodine concentration of 53.5 ± 19.5 mcg per 100g sample.
    - Additional data regarding the iodine content of infant formulae are also described in the Comprehensive Handbook of Iodine 2009, which should be considered and referenced.
- **Urinary iodine, urinary perchlorate, and serum thyroid hormones in the formula-fed infant:**
    - Leung et al 2012 publication: It should be noted that the report by Leung et al 2012 used in calibration of the model included both exclusively breastfed infants (35% of the sample size), as well as those who also partially consumed infant formula (65% of the sample size). This clarification is missing from Table 2 and in the corresponding text; it is a

significant limitation of the current model, as it assumes that all data was obtained from exclusively breastfed infants.

- Cao et al 2010 publication: Similarly, this report included both breastfed infants (46% of the sample size) and formula-fed infants (54% of the sample size), as noted in Table 2. The use of urinary iodine and perchlorate concentrations from this study for model calibration thus is not completely accurate when assuming they are resulting from exclusive breastfeeding or exclusive formula-feeding.

Michael H. Lumpkin, Ph.D., DABT

The report describes in detail the selection of data that serve as the basis of model parameter values for the various life stages. This includes the consideration of data published or made available since publication of the respective Lumen/Fisher/Clewell/McClannahan models. I am not aware of additional data that should be considered or preferentially utilized in the place of data described in the report.

Elizabeth N. Pearce, M.D., M.Sc.

Free T4 assays, as noted in the text, are poorly concordant with each other in pregnancy and some assays lose the expected inverse relationship with serum TSH values (Lee RH, Spencer CA, Mestman JH, Miller EA, Petrovic I, Braverman LE, Goodwin TM. Free T4 immunoassays are flawed during pregnancy. Am J Obstet Gynecol. 2009;200(3):260.e1-6.). It is generally recommended that normal thyroid function reference ranges be assay-specific, and that they should be defined in populations of individuals with no known history of thyroid disease, with adequate iodine intakes, and with negative thyroperoxidase (TPO antibodies). Among the studies used to derive free T4 reference values for the pregnancy BBDR models, the studies by Yan, Sticker et al. clearly met those criteria. The paper by Gong and Hoffman excluded TPO positive women; the sample was from Toronto, which likely means it was iodine sufficient. Similarly, the study by Wang et al. did not specify the study population's iodine status, although women were TPO Ab negative. In the study by Khalid et al., TPO antibody positivity was excluded and although urinary iodine was not ascertained, the study population, from Ireland, was most likely mildly to moderately iodine deficient. Additional data which could inform the definition of normal free T4 values in pregnancy are listed below under section 3A.

Hypothyroxinemia in lactating women, as noted above, is not currently considered a clinical adverse outcome, and thus there is essentially no literature on this entity. After the first 2-3 weeks postpartum (when levels are equilibrating after the changes of pregnancy), there is no reason to believe that reference intervals for free T4 should be any different in lactating women than they are for non-pregnant, non-lactating women. Unlike in pregnancy, there is not a strong hormonal driver for increased thyroid hormone production or metabolism. The amount of thyroid hormone secreted in breast milk is negligible (van Wassenaer AG, Stulp MR, Valianpour F, Tamminga P, Ris Stalpers C, de Randamie JS, van Beusekom C, de Vijlder JJ 2002 The quantity of thyroid hormone in human milk is too low to influence plasma thyroid hormone levels in the very preterm infant. Clin Endocrinol (Oxf) 56(5):621-627). Therefore, it should be possible to use the broader dataset for TPO negative, age-matched, non-pregnant

women from NHANES as well as data from other published sources to inform reference ranges for free T4 in the women who are lactating. The model currently uses data from only 39 lactating women from NHANES 2007-2008 and 2009-2010; this data set is very small and may include women with thyroid autoimmunity. Excluding TPO antibody positive women in the validation datasets for lactating women is particularly important because up to 10% of women experience postpartum thyroiditis, which will alter thyroid function values.

Decreasing excretion of urinary iodine in seven women over time was noted by Aboul-Khair et al. in data used to inform urinary iodine values for lactating women in the BBDR model. I am not able to access this paper, but have concerns about both the very small sample size and about what was known about the underlying iodine sufficiency of the women studied. Trends over the course of the first 90 days postpartum might be quite variable depending on ongoing iodine intake and presence or absence of adequate intrathyroidal iodine stores.

Table 6: The fractional kidney blood flow in third trimester women is assumed to be the same as for lactation. However, glomerular filtration rates and renal plasma flow are thought to be substantially increased in pregnancy (Dunlop W. Serial changes in renal hemodynamics during normal human pregnancy. Br J Obstet Gynaecol. 1981;88(1):1–9.).

Table 8: The free fraction of total T4 was estimated at 9×10^{-5} whereas it is estimated as 1×10^{-4} in lactating women. These fractions do not appear to fit with the knowledge that thyroxine binding globulin concentrations are increased twofold in pregnancy (Ain KB, Mori Y, Refetoff S. Reduced clearance rate of thyroxine-binding globulin (TBG) with increased sialylation: a mechanism for estrogen-induced elevation of serum TBG concentration. J Clin Endocrinol Metab. 1987;65(4):689.).

Page 43: it is noted with respect to the model for lactating women that "the clearance rate for metabolism or deiodination of T4 was set equal to the value for pregnant women.": This is likely inappropriate; given the high levels of type 3 deiodinase found in the placenta, the rate of thyroid hormone metabolism would be expected to be higher in pregnancy than in lactation. Page App-12: It its stated that "while there was uncertainty regarding the urinary clearance of perchlorate in lactating women vs. non-lactating women, there were no data or known biological reasons to expect it to be significantly different": this assumption is reasonable. However, on page App-17 it is noted that "maternal clearance of perchlorate is assumed to be lower during pregnancy": it seems more likely that the opposite would be true, given increased glomerular filtration rates in pregnant women.

Stephen M. Roberts, Ph.D.

Citations are provided for physiological and kinetic parameters taken from published sources. There are numerous data gaps for physiological and kinetic parameters, and these are discussed in the section on BBDR Model Development and Parameterization (beginning on page 22) in the context of the rationale for selection of various specific values. I have no substitute values to suggest.

Joanne F. Rovet, Ph.D.

The SAB-PAP report stressed the need to look at pregnancy and fetal thyroid function as key sensitive stages. Current authors maintain they did not include these stages as the relevant data for modelling are not available. This is surprising as much data exist on maternal thyroid levels and fetal data are available in the work of Thorpe-Beeston and on preterm infants (e.g., see work of Hume and Williams). Data too from the Rotterdam, Chinese, and Scandinavian cohorts could likely fill in a number of gaps. Authors need to see the paper by Peter Taylor et al (2014) on perchlorate in pregnancy and offspring IQ. Authors do extrapolate results to pregnant women and fetus, but I am not sure how this is done and when in pregnancy or fetal development this represents.

Question 1C. While the model predicts the dose-response for fetal thyroid hormones, a reference range for the fetus was not identified. Are there additional data, parameters, or (sub)models available that might be useful for evaluating fetal effects? If not, can the predictions for thyroid hormone changes in the pregnant mother be used as a measure of potential fetal effects?

Hugh A. Barton, Ph.D.

This reviewer cannot comment on this question.

Claude Emond, Ph.D.

This limitation regarding the reference range for the fetus might be an issue. It is discussed in the current draft review. As far as I know, there is not another reference that the authors might have forgotten to include in the PBPK model that suggests the possibility to describe the interaction of the fetus with the T3 and T4 hormones during gestation. This might be an issue; therefore, I believe that the reference range for the fetus should be part of the recommendation to generate data. T3 and T4 are highly important hormones in general development, including the brain. A lower concentration of fT4 and T4 resulting from perchlorate disruption would be an important issue to resolve.

Dale Hattis, Ph.D.

The emphasis on a "reference range" for hormone levels is, I think, a mistake. The implication is that values within the reference range carry no risk of harm and concern for adverse effects only arises if an individual who would ordinarily be in the reference range is moved by an exposure outside of the range. In fact, the most recently published analysis of data from a large prospective study[6] suggests that there is an optimum level of maternal free thyroxine for neurodevelopment, and a continuous form for changes in later IQ with both upward and downward departures from this optimum:

[6] Op. cit, ref. 1 above.

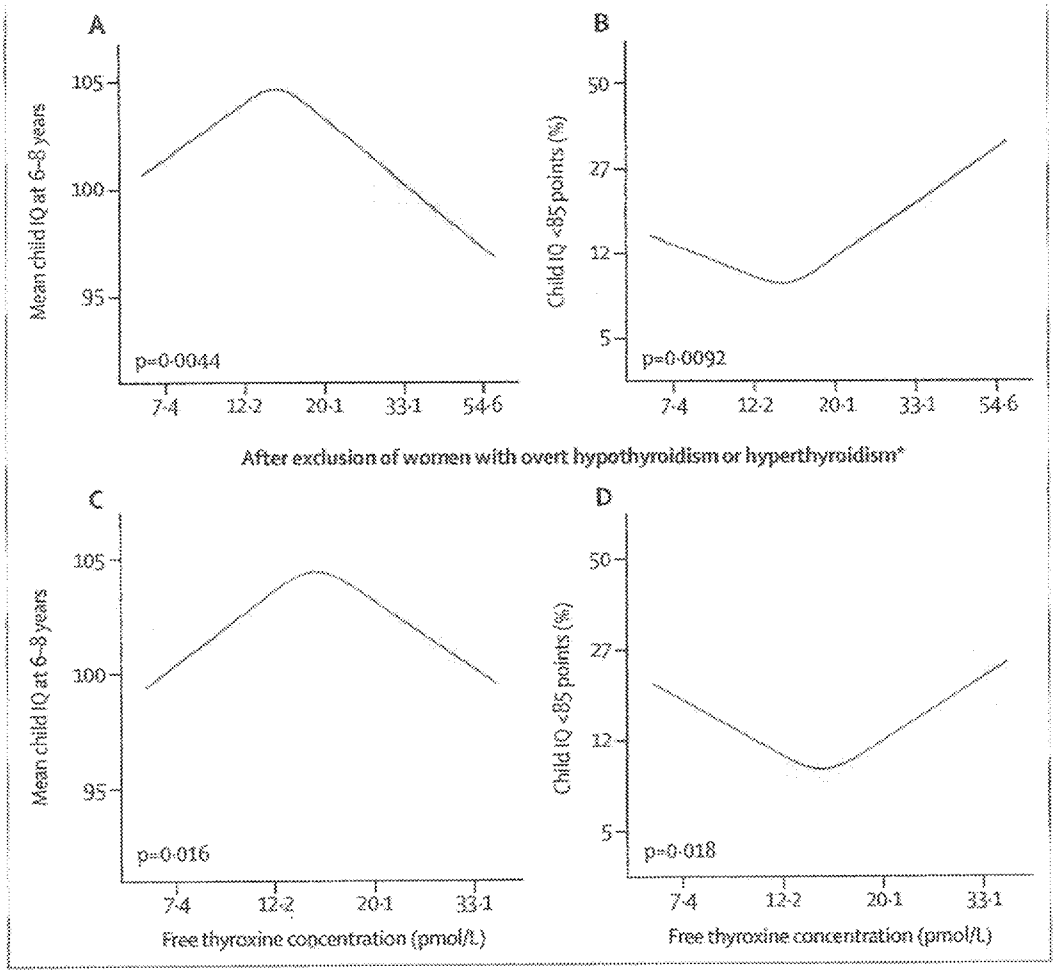


***Figure 2:* Association between maternal free thyroxine and offspring IQ**
(A, C) Association between maternal free thyroxine concentrations during pregnancy and child IQ as predicted mean and 95% CI in the whole population (A) and after the exclusion of women with overt thyroid disease (C). (B, D) Association of maternal free thyroxine levels during pregnancy and the risk of child IQ below 85 as predicted back-transformed log odds with 95% CI in the whole population (B) and after the exclusion of women with overt thyroid disease (D). Scales for the x-axis might differ between the upper and lower graphs because of exclusions of women with overt, but not subclinical, disease entities. Appendix p 5 provides effect estimates from standard linear regression models. IQ=intelligence quotient. *Overt hypothyroidism and hyperthyroidism are defined as the biochemical diagnosis made during pregnancy, based on the central 95% reference range, as advocated in international guidelines.

Source: Korevaar et al., ref. 1 above.

It must be noted that these plots have logarithmic axes for the independent variable, free thyroxine concentration. This means that if the relationships were plotted on linear axes, the lines to the left of the optima would appear much steeper than the lines to the right of the optima. The net effects need to take into account both the baseline population distribution and the net changes expected both to the left and the right of the optima.

Angela M. Leung, M.D., M.Sc.

Comments regarding fetal thyroid hormone concentrations:

The model's primary outcome is hypothyroxinemia as mediated by iodine status. However, hypothyroxinemia in the fetus was not able to be estimated by the current model, due to the inavailability of "in utero" fetal FT4 reference ranges in the current literature.

The fetus is one of the population subgroups who may be particularly susceptible to perchlorate exposure, given its biologic action on thyroidal iodine availability and therefore thyroid hormone production and brain development. Brain development in utero begins as early as 5 gestational weeks (Berbel et al; PMID 17962037). As the fetal thyroid gland is not functional until approximately 18-20 gestational weeks (Smallridge RC et al; PMID 11397821), normal brain dependent in the fetus is completely reliant on maternal transplacental passage of adequate thyroid hormone. However, even at 5 gestational weeks, the fetal thyroid is immature and thus continues to depend on maternal thyroid hormone throughout the rest of gestation, such that up to 50% of fetal T4 at delivery is that which is derived from the mother. As such, predictions of maternal thyroid hormone changes during pregnancy can serve as only a partial measure of thyroid hormone status in the fetus.

Michael H. Lumpkin, Ph.D., DABT

I am not aware of additional data, parameters, or submodels available that might be useful for evaluating fetal effects independent of the maternal effects. Historically, the use of maternal internal dosimetry and pharmacodynamics have been accepted as adequate surrogates for fetal internal doses or effects, are preferable to using maternal administered dose for extrapolation to fetal effects.

Elizabeth N. Pearce, M.D., M.Sc.

Fetal thyroid function cannot be directly measured without risk to the pregnancy. Therefore, there are no human studies examining fetal thyroid function. I think it is entirely reasonable to use maternal thyroid function as a proxy, especially given the data for adverse child developmental effects in association with early gestation maternal hypothyroxinemia. As noted above, however, I think it is important to extend the BBDR model to cover the first and second trimesters of pregnancy because there are currently no data for associations between third-trimester maternal hypothyroxinemia and adverse developmental outcomes.

It is also worth noting the recent study by Taylor et al (Taylor PN, Okosieme OE, Murphy R, Hales C, Chiusano E, Maina A, Joomun M, Bestwick JP, Smyth P, Paradice R, Channon S, Braverman LE, Dayan CM, Lazarus JH, Pearce EN. Maternal perchlorate levels in women with borderline thyroid function during pregnancy and the cognitive development of their offspring: data from the Controlled Antenatal Thyroid Study. J Clin Endocrinol Metab. 2014;99(11):4291-8.) in which we found that in an iodine-deficient cohort maternal urinary perchlorate levels in the highest 10% increased the odds of offspring IQ at age 3 being in the lowest 10%, with a greater adverse impact observed for verbal IQ than for performance IQ. Maternal levothyroxine

therapy did not appear to reduce the negative impact of perchlorate on offspring IQ. These data require confirmation in larger cohorts, and are perplexing because previously no association between maternal thyroid function and maternal urinary perchlorate concentrations were observed in this cohort (Pearce EN, Lazarus JH, Smyth PP, He X, Dall'amico D, Parkes AB, Burns R, Smith DF, Maina A, Bestwick JP, Jooman M, Leung AM, Braverman LE. Perchlorate and thiocyanate exposure and thyroid function in first-trimester pregnant women. J Clin Endocrinol Metab. 2010;95(7):3207-15).

Stephen M. Roberts, Ph.D.

Concern for the fetus as a sensitive life stage with respect to perchlorate effects is based in large part on observations of neurodevelopmental deficits among offspring of women who were thyroid deficient during pregnancy. The SAB Perchlorate Advisory Panel recommended that the EPA consider as a sensitive population the fetuses of hypothyroxinemic pregnant women; hence the need to develop a model capable of predicting the potential influence of perchlorate on hypothyroxinemia in pregnant women. Prediction of perchlorate effects on fetal thyroid hormones is not required in order to derive a perchlorate limit protective of neurodevelopmental effects from exposure during gestation. In fact, with the current state of knowledge, both attempts to estimate fetal thyroid changes and to quantify neurodevelopmental effects as a result of those changes would be highly uncertain.

Joanne F. Rovet, Ph.D.

See above. As a writer of the SAB-PAP report, I find this lack of data very disappointing. Yes, thyroid hormone changes in the pregnant mother can be used as a measure of potential fetal effects, especially in early pregnancy when the mother is the sole source of thyroid hormone for the fetal brain – and mothers' levels are known. Also, data from studies of preterm infants by the Scottish group under Hume and Williams can indicate thyroid-hormone capacity of the fetus in the third trimester.

Question 2. Modifications to existing models: EPA has modified one parameter in the 2013 Lumen et al. model: KM_TPNG, the Michaelis-Menten constant for the sodium-iodide symporter for perchlorate based on Schlosser (2016), and a second key parameter in the 2009 USEPA/2007 Clewell et al. PBPK models: VMAXC_MKP, the maximal velocity for perchlorate transfer to breast milk from those components in the USEPA 2009 models. These two parameters affect perchlorate transport from the mammary plasma to breast milk (VMAXC_MKP) and the strength with which perchlorate inhibits iodine transport by the sodium-iodine symporter (KM_TPNG). Detailed information on the assumptions and data considered in making these changes are provided in the report appendices. Are the changes scientifically supported and reasonably estimated?

Hugh A. Barton, Ph.D.

The change in Km value published in Schlosser (2016) is a reasonable scientifically supported reanalysis of the data used to establish that value. The logic presented of how the previous analysis had obtained the original Km value and the approach looking across the range of the available data is appropriate. Assuming this value to be life stage independent is an assumption, but a reasonable one absent other information.

It is more challenging to evaluate the change in VMAXC_MKP as the data are fairly scattered and addressing the range of perchlorate in milk versus urinary excretion required adjustments to other parameters, QMWB, mammary blood flow and PAMKC-P, passive diffusion of perchlorate. The approach appears reasonable, though absent working with the model directly it is difficult to have a clear perspective.

Claude Emond, Ph.D.

Lines 2 through 8, page 45

- The affinity constant (Km) for binding of perchlorate to the sodium-iodide symporter (NIS) (KM_TPNG) was reduced from 1.6×10^5 ng/L to 6×10^4 ng/L (Schlosser, 2016) because the in vitro data were reanalyzed (Kosugi et al., 1996). The same report suggests that making this modification results in a better prediction of the radioiodine uptake inhibition data from Greer et al. (2002) for the dose of 100 µg/kg/d than the simulation observed with the previous Km.

Lines 17 through 23, page 45

- Vmax for perchlorate transport from the mammary plasma to the milk call (VMAXC_MKP) also had a significant impact on model predictions. The authors were precise because they increased this value from the original model by a factor of 2.24; however, in the code file, they referred to this change because of ''P. Schlosser paper (2016)''. It should be referenced on page 45, line 23.
- As mentioned by the authors of this report, two parameters (i.e., VMAXC_MKP and KM_TPNG) are very sensitive.

- Rather than just mentioning it, the authors should further discuss these two parameters in the report. In addition, a sensitivity analysis of these two values should be included in the Sensitivity Analysis section, but they are not.

Dale Hattis, Ph.D.

First, given that these parameters are important determinants of the ultimate behavior of the pharmacokinetic model, it is a serious mistake to represent them as point estimates without estimates of either uncertainty nor variability distributions and analyses of the implications of these for policy-relevant outcomes.

The affinity of the symporter for iodide (KM_TPNG) appears to have been derived by picking a value and subjectively evaluating fit to the Greer data (App-11, Figure B-5). The new value clearly provides a better fit than the older value which was apparently based on fitting only the lowest point in the Greer data set. However, it seems to me that the fit could and should be further improved by a formal minimization of the statistically weighted departure of the model predictions from the data. Generally, the weighting for the data points should be based on the inverse of the uncertainty variance in either linear or log space depending on whether the sources of the errors in the data appear to be combine in an additive or a multiplicative way

Angela M. Leung, M.D., M.Sc.

Comments regarding modifications to existing models:

The modifications as summarized on pages 44-45 and Appendix B were reviewed. The two main modifications were the reduction of the affinity constant (Km) for the binding of perchlorate to NIS and the increased Vmax value for the transport of perchlorate from mammary plasma to breastmilk. This technical modeling aspects of this report are not my area of expertise, and thus I cannot comment on whether these are scientifically supported and/or reasonably estimated.

Michael H. Lumpkin, Ph.D., DABT

The justifications for modifying the NIS Michaelis-Menton constant (KM-TPNG) downward and adjusting blood-to-milk perchlorate transport velocity (VMAXC_MKP) using more robust data are sufficiently supported in the model report by the available data. Given the model structure changes required to align the perchlorate PBPK and iodine BBDR models, the need to revisit the model's fidelity to replicate the Greer et al. data was warranted. EPA noted that the non-pregnant female ("adult") model does not adequately replicate the RAUI behavior reported by Greer et al. for perchlorate doses above the RfD POD of 7 µg/kg/day. The strategy to begin by comparing the resulting Vmax values obtained for the older models using graphical methods to transform the data to linear relationships (as was done by Kosugi et al. [1996]) with novel fitting of the Kosugi et al. *in vitro* data using modern non-linear fitting techniques makes sense. The newly fitted Vmax value resulted in far better concordance of the model-predicted RAUI for non-pregnant women with the Greer et al. data. The EPA approach to testing the

performance of the lactating mother model with the revised KM-TPNG value was also reasonable, utilizing gestation week 38 iodide burdens as the initial conditions to simulate the Greer et al. experiment.

The use of the newer and more robust breast milk/urinary perchlorate concentration data of Kirk et al. (2013), compared to that of Tellez et al. (2005) to calibrate the rate of transport of perchlorate and iodine into breast milk was adequately justified din the report. EPA showed that the Kirk data provide more detailed and statistically powerful information with which to explore the relationship between perchlorate elimination to breast milk or urine in the lactating mother. The use of the multiplicative factor vmult to scale mammary blood flow with mammary Vmax for perchlorate adequately captured the extreme values of mammary elimination of perchlorate in the Kirk et al. study population.

Elizabeth N. Pearce, M.D., M.Sc.

The decision to eliminate the thyroid lumen as a separate model compartment seems reasonable, as does the decision to simplify the model to allow transport directly from mammary plasma to the breast milk. I also agree that it is reasonable to assume that the Km for iodine and for perchlorate are the same for NIS in the breast as they are for NIS in other tissues. It is reasonable to assume that the perchlorate urinary clearance will be the same in lactating women as in non-pregnant, non-lactating women.

The revised $Km_{NIS,ClO4}$ based on the re-analysis of the Kosugi (1996) paper is based on reasonable assumptions, however, given that the original Kosugi data were not actually available, the calibration of the model against existing datasets (see below) is particularly critical.

Stephen M. Roberts, Ph.D.

Explanations for the changes in parameters VMAXC_MKP and KM_TPNG are provided in Appendix B. The rationale and procedure for the change in KM_TPNG is reasonable and scientifically supported. The narrative describing the rationale and procedure for the change in VMAXC_MKP is more difficult to follow. Without additional explanation, I am unable to determine whether this change is scientifically supported and reasonably estimated.

Joanne F. Rovet, Ph.D.

These seem reasonable to me.

Question 3. Model calibration and sensitivity analysis: Please address the strengths and limitations of the model calibration process and the strengths and limitations of the data used for model calibration and evaluation. Identify any additional literature, data, or peer reviewed models that EPA should consider to address identified limitations.

Hugh A. Barton, Ph.D.

The strategy described for calibrating the formula fed infant first followed by the breast-fed infant and nursing mother is a logical one since the formula fed infant would be independent of the maternal parameters after birth.

Claude Emond, Ph.D.

No comment here.

Dale Hattis, Ph.D.

The fitting described in Appendix B appears to have been done without formal statistical optimization one parameter at a time, sometimes (as in the case of the Vmax value for the symporter transfer) accompanied by adjustment of another parameter, in that case the " permeability-area constant for diffusional transfer" (App 15, line 16). On the following page further individual ad hoc adjustments are described to mammary blood flow. When the values of multiple parameters are being tweaked and fits evaluated against multiple and diverse sets of observational data, I have found it to be helpful to have a much more formal search process with simultaneous variation of all the adjustable parameters and evaluation of overall fit considering the inverse-variance weighted departures of the model predictions from all the observational data sets being considered. Otherwise, the repeated adjustment of all the model parameters becomes just too complicated for me to trust my subjective judgment of fit.

Angela M. Leung, M.D., M.Sc.

Comments regarding the model calibration process and sensitivity analysis:

a. Model calibration
   - Calibration has been attempted to be done utilizing the available data from the literature regarding iodine, perchlorate, and thyroid hormone measurements in lactating women and infants. However, some of the data are misinterpreted (see my responses to Question 1B) or missing; thus, the model contains some calibration parameters that may be inexact, particularly for breastmilk and urinary iodine concentrations.
   - The statements regarding the instability of iodine levels in breastmilk on page 64 line 9 and page 82 lines 10-13 are likely misinterpretations of the personal communications with Dr. Blount, as iodine is an extremely stable element and their concentrations are unlikely to change within such short timeframes.
b. Model sensitivity analysis
   - Please see my responses below in Question 3B.

Michael H. Lumpkin, Ph.D., DABT

Strengths of the data set utilized for model calibration and evaluation include the use of data from the actual human population (including the most sensitive sub-population) for which health risks a will be evaluated. Further, the data for iodide, perchlorate, and thyroid hormone levels that was used for model evaluation are in the approximate concentration space (0-20 µg/kg/d perchlorate; 9-16 pM serum fT4) for which the model was intended *a priori*.

Elizabeth N. Pearce, M.D., M.Sc.

Strengths of the model calibrations and sensitivity analysis process include attention to validating the model against carefully-selected representative data for each life stage, and testing over a range of assumed iodine and perchlorate exposures.

It was reasonable to exclude neonatal data from the first 7 days of life in model calibrations due to the difficulty of dealing with effects of the neonatal TSH surge.

The primary weaknesses of the model calibration process was the limited nature of the datasets against which model was validated. Suggestions for additional studies are below (3A).

Leung et al. (2012) was used as the primary data source for deriving NIS-mediated uptake of iodine into breast milk. It is notable that breast milk iodine concentrations among the women in that study were extremely variable, and that the number of exclusively breastfed infants was quite small. As we concluded in that study, timing of breast milk sampling is likely one factor which explains some of the variability in measured samples; we have shown that breast milk content peaks at 6 hours after a mother ingests an iodine load. The model assumes a constant rate of iodine excretion into breast milk, which is not the case, and may complicate efforts at model calibration.

Stephen M. Roberts, Ph.D.

I will defer to other panel members on the calibration process.

Joanne F. Rovet, Ph.D.

I am not too familiar with this literature but it seems to me that most of the papers I could find are cited or authored by members of the modeling team. This is definitely an area of strength of the modelers.

Question 3A. Specifically, is the model calibration and evaluation adequately compared with what is reported in the literature for iodine and perchlorate concentrations in urine, and breast milk and thyroid hormone plasma concentrations under different iodine intake and perchlorate exposure scenarios? Please identify additional studies that would support model calibration that strengthen the proposed model.

Hugh A. Barton, Ph.D.

The model simulations shown in Figures 4 – 9 seem reasonable with some of the discrepancies as described in the report.

A challenge for this calibration is that there are other factors contributing to the observed population variability that are not incorporated into the model (e.g., variability in PK determinants like NIS for iodide and perchlorate handling, variability in thyroid hormone production and clearance, variability of intake for other NIS inhibitors potentially in diet or other sources). However, trying to add the variability into the model would only make sense if it appears to reasonably capture the average behaviors. Like any biologically based model attempting to simulate data across a wide range of endpoints from studies with different designs, some simulations are better than others. It is challenging to understand how well the available data determine the parameters that were fitted without doing a sensitivity analysis for each endpoint and study design. The variability may be important in that several studies did not find correlations among iodine and/or perchlorate levels and thyroid hormone levels (in either urine or plasma for different study designs) suggesting that other factors were contributing. The model has a deterministic description of perchlorate inhibition of iodine transport and the impact on thyroid hormone levels, so this could be perceived to be at odds with the data. It seems plausible, however, that there are other factors (some noted above) contributing to the variability that obscure relationships among iodine, perchlorate, and thyroid hormone absent exact accounting for co-variates or other approaches for population variability. This will make it challenging to use the modeling to establish a health protective level challenging and maintaining the credibility of the analysis. As noted, the easy answer, also suggested in some of the public comments, is to further expand the model to include these sources of variability, but that may not be so easy to do and demonstrate that the results are more strongly supported than the current analyses. This is an area that would benefit from at least qualitative discussion and clear acknowledgement of current limitations of the modeling, though there are not necessarily easy alternative approaches to apply that have fewer limitations.

Claude Emond, Ph.D.

I did not find any additional literature that may further support the authors' research regarding this model. I believe this report contains the major publications available.

Dale Hattis, Ph.D.

I think not. There needs to be a much more formal process of comparison of model predictions and observed data. Uncertainties in the data should be modeled and expressed as confidence limits, and summarized for comparison with model predictions.

Angela M. Leung, M.D., M.Sc.

Comments regarding model calibration and evaluation under different iodine and perchlorate scenarios:

Figures 4-9 report the model calibration results compared to data in the literature for iodine and perchlorate concentrations in urine and breastmilk and of serum thyroid hormone concentrations under different iodine intake and perchlorate exposure scenarios. As noted in my responses to Question 1B, there are some additional studies that should be reexamined and/or included to strengthen the calibration. Some specific comments are as follows:

- Figure 4 (Urinary iodine and perchlorate for formula-fed infants): It is reassuring that the model-predicted urinary iodine concentrations for formula-fed infants assumed to consume infant formula with the lowest iodine content (108 mcg/L) was within the range of urinary iodine concentrations range reported in the literature for infants fed both cow milk-based and soy-based infant formulas, but as mentioned previously, additional studies could be included regarding the iodine content of infant formulae. For infant formulas with the highest iodine content (384 mcg/L), model-predicted urinary iodine concentrations were only within the range of those consuming cow milk-based formula, which is reasonable. Model-predicted urinary perchlorate concentrations were within the range of those reported in the literature for the perchlorate content of cow milk- and soy milk-based infant formulas.
- Figure 5 (Urinary iodine for breastfed infants): The model-predicted urinary iodine concentrations for breastfed infants are also within the range of those reported in the literature at postnatal days 45-90, although as noted previously, there are limitations to the calibration of breastmilk and urinary iodine concentrations used in the model. Average maternal perchlorate dietary intake was estimated and assumed to be 100 ng/kg/day for these calibrations. Also noted is that the model for urinary iodine in breastfed infants is not within the range of literature data for postnatal days 7-44, a similarly critical period of rapid infant neurodevelopment.
- Figure 6 (Urinary perchlorate for breastfed infants): These calibrations appear to be reasonable and within the range of literature-reported values among both formula-fed and breastfed infants from postnatal days 0-90, although as noted previously, there are limitations to the calibration of breastmilk and urinary perchlorate concentrations used in the model. Maternal dietary iodine intake between 75-250 mcg/day had no effect on predicting urinary perchlorate concentrations in their breastfed infants.
- Figure 7 (Breastmilk iodine and perchlorate): The potential issues of calibration against the published literature data is summarized above in Question 1B regarding the significant variability of breastmilk iodine content in relation to dietary iodine intake.

- Figure 8 (Maternal serum TT4 and FT4): The model-predicted values are comparable to existing literature from NHANES cohorts, but significant limitations include the lack of assessment of thyroid autoantibody positivity and other variables (see my responses to Question 1B), as well as the extremely small size of this cohort upon which the model is based. Model simulations were performed for maternal dietary iodine intakes from 75-250 mcg/day and an assumed maternal perchlorate exposure of 100 ng/kg/day.
- Figure 9 (Serum TT4 and FT4 for breastfed infants; no literature available for formula-fed infants): The model-predicted serum thyroid hormone values are comparable to existing literature, although as noted previously, there are limitations to the calibration of serum thyroid hormone concentrations used in the model. Although a maternal dietary intake of 75 mcg/day predicts serum TT4 and FT4 concentrations much lower than those for higher dietary iodine intakes (150-250 mcg/day), the serum thyroid hormone concentrations of their breastfed infants remain within the range during postnatal days 7-90.

Michael H. Lumpkin, Ph.D., DABT

The model appears to adequately predict iodide, perchlorate, and thyroid hormone levels in various matrices in all of the evaluated life stages. In the lactating mother, the model captured well the observed postpartum levels of iodide and perchlorate in milk (reflecting the performance of the NIS M-M parameters, as adjusted for this model) as well as serum fT4 levels that are in the range (9-12 pM) for which dose-response analyses were recommended. The same appears to hold true for urinary iodide and perchlorate and serum fT4 simulations in breast-fed infants.

Elizabeth N. Pearce, M.D., M.Sc.

Studies with trimester-specific thyroid function reference ranges (all studies excluded TPO antibody positive women):

Bocos-Terraz JP, Izquierdo-Alvarez S, Bancalero-Flores JL, Alvarez-Lahuerta R, Aznar-Sauca A, Real-López E, Ibáñez-Marco R, Bocanegra-García V, Rivera-Sánchez G. Thyroid hormones according to gestational age in pregnant Spanish women. BMC Res Notes. 2009;2:237. *[cohort is mildly iodine deficient]*

Gilbert RM, Hadlow NC, Walsh JP, Fletcher SJ, Brown SJ, Stuckey BG, Lim EM. Assessment of thyroid function during pregnancy: first-trimester (weeks 9-13) reference intervals derived from Western Australian women. Med J Aust. 2008;189(5):250-3. *[borderline iodine deficient cohort]*

Lambert-Messerlian G, McClain M, Haddow JE, Palomaki GE, Canick JA, Cleary-Goldman J, Malone FD, Porter TF, Nyberg DA, Bernstein P, D'Alton ME; FaSTER Research Consortium. First- and second-trimester thyroid hormone reference data in pregnant women: a FaSTER (First- and Second-Trimester Evaluation of Risk for aneuploidy) Research Consortium study. Am J Obstet Gynecol. 2008;199(1):62.e1-6 *[mildly iodine deficient cohort]*

La'ulu SL, Roberts WL. Ethnic differences in first-trimester thyroid reference intervals. Clin Chem. 2011;57(6):913-5. *[mildly iodine deficient cohort]*

Zhang X, Yao B, Li C, Mao J, Wang W, Xie X, Teng X, Han C, Zhou W, Li C, Xu B, Bi L, Meng T, Du J, Zhang S, Gao Z, Yang L, Fan C, Teng W, Shan Z. Reference Intervals of Thyroid Function During Pregnancy: Self-Sequential Longitudinal Study Versus Cross-Sectional Study. Thyroid. 2016;26(12):1786-1793. *[iodine sufficient cohort]*

Pearce EN, Oken E, Gillman MW, Lee SL, Magnani B, Platek D, Braverman LE. Association of first-trimester thyroid function test values with thyroperoxidase antibody status, smoking, and multivitamin use. Endocr Pract. 2008;14(1):33-9. *[likely iodine sufficient or borderline cohort, but not assessed]*

Männistö T, Surcel HM, Ruokonen A, Vääräsmäki M, Pouta A, Bloigu A, Järvelin MR, Hartikainen AL, Suvanto E. Early pregnancy reference intervals of thyroid hormone concentrations in a thyroid antibody-negative pregnant population. Thyroid. 2011;21(3):291-8. *[iodine sufficient cohort]*

Bestwick JP, John R, Maina A, Guaraldo V, Joomun M, Wald NJ, Lazarus JH. Thyroid stimulating hormone and free thyroxine in pregnancy: expressing concentrations as multiples of the median (MoMs). Clin Chim Acta. 201;430:33-7. *[cohort is mildly-moderately iodine deficient]*

Medici M, de Rijke YB, Peeters RP, Visser W, de Muinck Keizer-Schrama SM, Jaddoe VV, Hofman A, Hooijkaas H, Steegers EA, Tiemeier H, Bongers-Schokking JJ, Visser TJ. Maternal early pregnancy and newborn thyroid hormone parameters: the Generation R study. J Clin Endocrinol Metab. 2012;97(2):646-52. *[iodine sufficient cohort]*

Quinn FA, Gridasov GN, Vdovenko SA, Krasnova NA, Vodopianova NV, Epiphanova MA, Schulten M. Prevalence of abnormal thyroid stimulating hormone and thyroid peroxidase antibody-positive results in a population of pregnant women in the Samara region of the Russian Federation. Clin Chem Lab Med. 2005;43(11):1223-6. *[moderately iodine deficient cohort]*

Springer D, Zima T, Limanova Z. Reference intervals in evaluation of maternal thyroid function during the first trimester of pregnancy. Eur J Endocrinol. 2009;160(5):791-7. *[mildly iodine deficient cohort]*

Vaidya B, Anthony S, Bilous M, Shields B, Drury J, Hutchison S, Bilous R. Detection of thyroid dysfunction in early pregnancy: Universal screening or targeted high-risk case finding? J Clin Endocrinol Metab. 2007;92(1):203-7. *[mildly to moderately iodine deficient cohort]*

Studies investigating links between maternal hypothyroxinemia in pregnancy and aversechild developmental outcomes:

Craig WY, Allan WC, Kloza EM, Pulkkinen AJ, Waisbren S, Spratt DI, Palomaki GE, Neveux LM, Haddow JE. Mid-gestational maternal free thyroxine concentration and offspring neurocognitive development at age two years. J Clin Endocrinol Metab. 2012;97(1):E22-8.

Finken MJ, van Eijsden M, Loomans EM, Vrijkotte TG, Rotteveel J. Maternal hypothyroxinemia in early pregnancy predicts reduced performance in reaction time tests in 5- to 6-year-old offspring. J Clin Endocrinol Metab. 2013;98(4):1417-26.

Julvez J, Alvarez-Pedrerol M, Rebagliato M, Murcia M, Forns J, Garcia-Esteban R, Lertxundi N, Espada M, Tardón A, Riaño Galán I, Sunyer J. Thyroxine levels during pregnancy in healthy women and early child neurodevelopment. Epidemiology. 2013;24(1):150-7.

Ghassabian A, El Marroun H, Peeters RP, Jaddoe VW, Hofman A, Verhulst FC, Tiemeier H, White T. Downstream effects of maternal hypothyroxinemia in early pregnancy: nonverbal IQ and brain morphology in school-age children. J Clin Endocrinol Metab. 2014;99(7):2383-90.

Gyllenberg D, Sourander A, Surcel HM, Hinkka-Yli-Salomäki S, McKeague IW, Brown AS. Hypothyroxinemia During Gestation and Offspring Schizophrenia in a National Birth Cohort. Biol Psychiatry. 2016;79(12):962-70.

Modesto T, Tiemeier H, Peeters RP, Jaddoe VW, Hofman A, Verhulst FC, Ghassabian A Maternal Mild Thyroid Hormone Insufficiency in Early Pregnancy and Attention-Deficit/Hyperactivity Disorder Symptoms in Children. JAMA Pediatr. 2015;169(9):838-45.

Korevaar TI, Muetzel R, Medici M, Chaker L, Jaddoe VW, de Rijke YB, Steegers EA, Visser TJ, White T, Tiemeier H, Peeters RP. Association of maternal thyroid function during early pregnancy with offspring IQ and brain morphology in childhood: a population-based prospective cohort study. Lancet Diabetes Endocrinol. 2016;4(1):35-43.

Additional data for U.S. infant formula iodine and perchlorate concentrations can be found in:

Pearce EN, Leung AM, Blount BC, Bazrafshan HR, He X, Pino S, Valentin-Blasini L, Braverman LE. Breast milk iodine and perchlorate concentrations in lactating Boston-area women. J Clin Endocrinol Metab. 2007;92(5):1673-7.

The following study includes data on radioactive iodine uptakes following ingestion of perchlorate doses ranging from 0.5 mg/d to 3 mg/d in healthy volunteers and could be another source, in addition to Greer et al, to use for model validation:

Braverman LE, Pearce EN, He X, Pino S, Seeley M, Beck B, Magnani B, Blount BC, Firek A. Effects of six months of daily low-dose perchlorate exposure on thyroid function in healthy volunteers. J Clin Endocrinol Metab. 2006;91(7):2721-4.

A new balance study in formula-fed 2-month-old infants is highly relevant:

Dold S, Zimmermann MB, Baumgartner J, Davaz T, Galetti V, Braegger C, Andersson M. A dose-response crossover iodine balance study to determine iodine requirements in early infancy. Am J ClinNutr. 2016 Sep;104(3):620-8.

The following studies have examined maternal thyroid function in relation to iodine and perchlorate exposure in pregnancy (at various stages of gestation) and might be used to help with model calibration, especially if, as I would recommend, the model is expanded to examine the first two trimesters of pregnancy:

Steinmaus C, Pearl M, Kharrazi M, Blount BC, Miller MD, Pearce EN, Valentin-Blasini L, DeLorenze G, Hoofnagle AN, Liaw J. Thyroid Hormones and Moderate Exposure to Perchlorate during Pregnancy in Women in Southern California. Environ Health Perspect. 2016;124(6):861-7.

Charatcharoenwitthaya N, Ongphiphadhanakul B, Pearce EN, Somprasit C, Chanthasenanont A, He X, Chailurkit L, Braverman LE. The association between perchlorate and thiocyanate exposure and thyroid function in first-trimester pregnant Thai women. J Clin Endocrinol Metab. 2014;99(7):2365-71.

Pearce EN, Alexiou M, Koukkou E, Braverman LE, He X, Ilias I, Alevizaki M, Markou KB. Perchlorate and thiocyanate exposure and thyroid function in first-trimester pregnant women from Greece. Clin Endocrinol (Oxf). 2012;77(3):471-4.

Pearce EN, Spencer CA, Mestman JH, Lee RH, Bergoglio LM, Mereshian P, He X, Leung AM, Braverman LE. Effect of environmental perchlorate on thyroid function in pregnant women from Córdoba, Argentina, and Los Angeles, California. Endocr Pract. 2011;17(3):412-7.

Pearce EN, Lazarus JH, Smyth PP, He X, Dall'amico D, Parkes AB, Burns R, Smith DF, Maina A, Bestwick JP, Jooman M, Leung AM, Braverman LE. Perchlorate and thiocyanate exposure and thyroid function in first-trimester pregnant women. J Clin Endocrinol Metab. 2010;95(7):3207-15

Horton MK, Blount BC, Valentin-Blasini L, Wapner R, Whyatt R, Gennings C, Factor-Litvak P. Co-occurring exposure to perchlorate, nitrate and thiocyanate alters thyroid function in healthy pregnant women. Environ Res. 2015;143(Pt A):1-9.

Mortensen ME, Birch R, Wong LY, Valentin-Blasini L, Boyle EB, Caldwell KL, Merrill LS, Moye J Jr, Blount BC. Thyroid antagonists and thyroid indicators in U.S. pregnant women in the Vanguard Study of the National Children's Study. Environ Res. 2016;149:179-88.

Stephen M. Roberts, Ph.D.

The process for identifying papers for calibration and evaluation should be explained more fully. Some of the exclusion criteria (e.g., mothers and infants that did not have sufficient iodine in their diets) could have eliminated studies useful for evaluating model accuracy in estimating thyroid hormone levels for individuals with low iodine intake. Also, the description of the

process indicates that 62 articles were identified that had data used for calibration, validation or setting model parameters, but concludes with the statement that "The review process was halted after it was judged that the objective had been met; i.e., sufficient data for model calibration had been identified." This suggests that articles with information potentially useful for calibration or evaluation were not considered.

Joanne F. Rovet, Ph.D.

YES for iodine and perchlorate and breast milk. NO for thyroid hormone/iodine and perchlorate. However, as I found the Results section messy and not clear, I cannot adequately judge how well the model agrees with the extant literature for iodine and perchlorate concentrations in urine and breast milk. The only study to examine these is Leung et al. (2012), which found no effect of breast milk perchlorate on infant thyroid hormone levels.

Question 3B. Are the influential parameters identified in the local sensitivity analysis for total thyroxine (T4) and free thyroxine (fT4) plasma concentrations consistent with known biology? Are there critical data gaps for the influential parameters, which would impact the thyroid hormone predictions? If gaps are identified, please provide approaches that would improve thyroid hormone predictions.

Hugh A. Barton, Ph.D.

This reviewer cannot comment on whether the "influential parameters" are "consistent with known biology". There are descriptions in Tables 4 and 5 of the basis for the values for these influential parameters and there does appear to be some data available for each, though it is difficult to evaluate how well it determines each parameter.

Claude Emond, Ph.D.

The sensitivity analysis (SA) discussed in the report tested the influence of the new parameters, which were also described for the iodine description, and discussed whether there was a presence of exogenous perchlorate and iodine. The analysis and synthesis performed in this report are not descriptive enough. The report should include more detailed discussions so the readers will understand the impact of each parameter. Currently, based on the SA each parameter seems to have a similar impact in the prediction of the model. It is difficult to extract the sensitive parameters that drive the simulation.

Dale Hattis, Ph.D.

The influential model parameters seem to have been identified, but I am not satisfied with the generally subjective procedures used to judge whether the existing set of parameter values leads to model predictions that reasonably correspond to model predictions, or whether better model predictions are possible using improved sets of parameter values.

Angela M. Leung, M.D., M.Sc.

Comments regarding sensitivity analyses for serum TT4 and FT4 concentrations:
The analyses reported on pages 83-91were reviewed, from which the main findings are summarized as below.

- Results for infant serum TT4 and FT4 concentrations are identical, and thus only infant serum T4 concentrations are reported.
- Influential parameters were time-dependent, iodine-dependent, and perchlorate-dependent.
- Given the relatively lower iodine content in breastmilk, as compared to infant formula, the effect of perchlorate exposure was more significant in the analyses which examined perchlorate exposure from breastmilk.

These findings are generally consistent with the available knowledge regarding factors which may influence serum thyroid hormone concentrations. However, as described in my response to

Question 4A, it would be prudent to also examine the influence of serum thyroid autoantibody positivity on serum thyroid hormone concentrations in these sensitivity analyses.

Michael H. Lumpkin, Ph.D., DABT

Although the report states that the most influential parameters are time-, iodide-, and perchlorate-sensitive (p84), Figures 19-20 and Tables 11-12 do not seem to support this, except for the day 7 influence for both formula and breast-fed infants. The influence of daily T4 production (VPRODT4CX) and 1st order T4 clearance (CLMETT4CX) parameter values have far more impact than parameters that influence perchlorate-related changes to iodide transport into the thyroid and breast milk, which is surprising. If that is the case for this model, some discussion in the report of why that is the case may be helpful.

Elizabeth N. Pearce, M.D., M.Sc.

Sensitivity analyses used to determine influential parameters for total and free T4 concentrations in formula- and breast-fed infants included a range of iodine exposures (from 75-200 mcg daily for mothers and breastfed infants, and from 108-384 mcg/L formula for the formula-fed infants) and of perchlorate exposures (from 0-20 mcg/kg/day) for both mothers and infants. The range of perchlorate exposures chosen for testing seems reasonable. It should be noted that there is a very wide range of allowable infant formula iodine content for full-term infants in the U.S: 5 to 75 µg/100 kcal (33.5–507.2 µg/L) (U.S. Food and Drug Administration 2006Code of Federal Regulations 21CFR107 Infant formula. [HYPERLINK "http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=107&showFR=1"]). Therefore, the sensitivity analyses did not account for potentially much lower iodine exposures in formula-fed infants which presumably could occur in the U.S.

It is logical that rates of T4 to FT4 conversion, rates of T4 production in the infant thyroid, and rates of thyroid hormone metabolism would be the highly influential parameters for the FT4 models. In the breastfed infants, the influence of intrathyroidal iodine stores (CTGIPOOL_N) is a stronger influence at day 7 of life than at day 90; this makes sense in light of the fact that intrathyroidal iodine turnover is highest in the immediate neonatal period.

Stephen M. Roberts, Ph.D.

The results of the local sensitivity analysis are cryptic at best. Normalized sensitivity coefficients are presented in graphical and tabular form for parameters listed in coded form. There is virtually no discussion of parameters identified as influential, other than to say "influential parameters were time-dependent, iodine-dependent, and perchlorate-dependent." It would in fact be useful to clearly identify what are regarded as influential parameters and to discuss in the report whether they are consistent with known biology, but that is missing. As presented, the sensitivity analysis will have little value for most readers.

Joanne F. Rovet, Ph.D.

I am not able to answer this given the way the information is presented. I would have liked a closer match between the categories in Table 7 and the models in Figures 2 and 3.

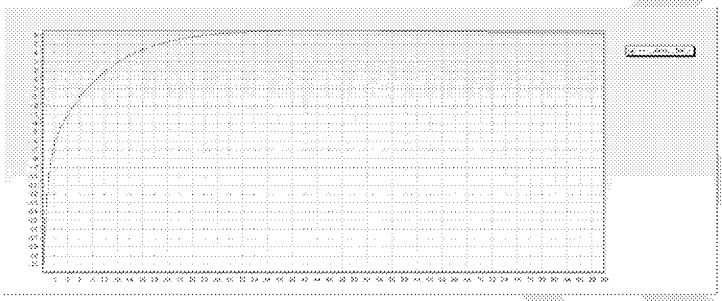
Question 3C. Does the proposed model provide the appropriate level of precision and substantiated support for this approach? Please identify any additional limitations of the model's applicability?

Hugh A. Barton, Ph.D.

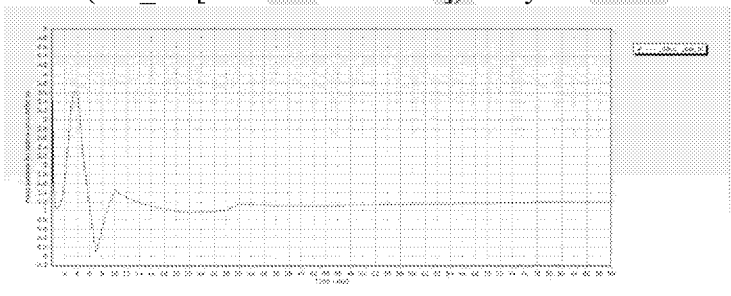
Presumably, "this approach" refers to using the model to assess potential perchlorate dose-response. Various limitations of the effort are noted in the report and the comments here.

Claude Emond, Ph.D.

The mass balance for the maternal iodine (Bal_i [see line 1561 of the code in acslX]) should be checked (see the figure below). For iodine, the mass balance is probably a minor error, but it should be corrected.



As can be seen in the figure below, there is also an issue regarding the mass balance for the infant (Bal_Ni [see code line 1577]). Maybe a correction or justification is required.



The mass balance for the weight and the volume are both fine for the mother and the infant.
I am unsure why the authors doubled the volume and the blood flow for perchlorate and iodine?

Dale Hattis, Ph.D.

This cannot be adequately evaluated with the comparison plots provided.

Angela M. Leung, M.D., M.Sc.

Comments regarding model precision:

There are several limitations, as mentioned elsewhere in this report, which may limit the precision and substantiated support of the model.

In addition, there was a recent publication estimating the perchlorate burden from dietary intake as part of the FDA's Total Diet Study (Abt E et al, PMID 28000685), which can be cited to support the range of perchlorate exposure levels assessed in the model.

Michael H. Lumpkin, Ph.D., DABT

The performance of the model in replicating concurrent milk and urine iodine and perchlorate data in the lactating mother, and perchlorate and serum fT4 in the breast-fed infant in the space of perchlorate exposure and thyroid hormone levels for which that model is intended be utilized indicates sufficient precision of the model for use in dose-response assessment.

Elizabeth N. Pearce, M.D., M.Sc.

I do not have expertise in model development, so I am unable to comment on this question.

Stephen M. Roberts, Ph.D.

It is difficult to determine from the report whether the model provides the appropriate level of precision and substantiated support for this approach. As presented in the report, model predictions of various outputs (e.g., urinary perchlorate, urinary iodide) typically fall within or near a broad range of values reported in the literature. One interpretation is that the model is consistent with empirical observations in humans. Another interpretation is that the model predictions could be substantially different and still be consistent with the literature given the variability observed there. This problem is not easily solved, as studies providing actual measurements are likely to have influences in play that contribute to the substantial variability that is observed, but are poorly understood and therefore cannot be captured in the model.

Joanne F. Rovet, Ph.D.

I was not able to fully comprehend the meaning of the data in Figures 18-20 or Tables 11-12 as they contained what seemed to me to be just raw data or statistical output with little attempt to synthesize these data. No statistics are presented and the Figures lack legends that might allow one to zero in on key findings. Global comparison of the three figures suggests to me a greater impact of perchlorate at Day 7 in the formula-fed than breast-fed infant at the low iodine level; in the mother, this perchlorate effect took place later. I am not sure how my "eye-balling" conforms with the graphs provided.

Question 4. Hypothyroxinemic reference levels and model predictions: The SAB (2013) recommended that the EPA focus the application of BBDR modeling on the condition of hypothyroxinemia, in which circulating levels of free thyroxine (fT4) are reduced below the normal ("reference") range, but with normal levels of thyroid stimulating hormone (TSH). While the mode of action (MOA) for perchlorate is well described, a defined set of quantitative definitions for reference ranges for hypothyroxinemia during pregnancy or lactation and in infants is not available. For interpretation of the BBDR model, EPA developed a normalization procedure to derive hypothyroxinemia reference intervals and to control for the expected differences between literature results and model predictions.

Question 4A. Please comment on the hypothyroxinemia reference ranges derived for pregnant mothers, fetuses, lactating mothers, breast-fed infants and bottle-fed infants. Is the assumed range between the 2.5th and 10th percentile of the fT4 distribution reasonable? Is it supported by the available data? Has the derivation of the reference ranges, including the normalization process, been appropriately described and supported in the model and the report?

Hugh A. Barton, Ph.D.

This reviewer cannot comment on the range of iodine intake levels beyond indicating that the approach of using a range of values appears a valuable one.

Claude Emond, Ph.D.

As mentioned in page 17 of the report, there has been no consensus in the literature regarding the limit between euthyroid and hypothyroxinemia condition; therefore, determining this by using the range of fT4 is reasonable.

Dale Hattis, Ph.D.

I think these choices of reference ranges are completely arbitrary and not founded without well-grounded justification in biology. As indicated earlier, I think it would be best to use the thyroid hormone predictions from exposures to perchlorate in early pregnancy to estimate expected population-wide changes in expected IQ's for the offspring of the pregnancies. This endpoint would provide much more meaningful information for juxtaposing expected costs and benefits of regulatory actions to alter perchlorate exposures.

Angela M. Leung, M.D., M.Sc.

Comments regarding hypothyroxinemia reference ranges:

Page 17 (lines 12-21) outlines the model's definition of hypothyroxinemia, which are described as serum FT4 concentrations for pregnant mothers, lactating mothers, breastfed infants, and formula-fed infants in the 2.5-10th percentile of the general population. Euthyroxinemia in the model is defined as serum FT4 concentrations in the 10-90th percentile. The selected reference range for hypothyroxinemia also assumes that overt hypothyroidism (i.e., an elevated serum TSH concentration with low serum FT4 concentration) occurs when serum FT4 concentrations are in the <2.5th percentile range. These parameters were chosen due to a lack of a universal definition for hypothyroxinemia in these population subgroups from the available literature. The following are some considerations, particularly regarding the limitations surrounding the definition of hypothyroxinemia during pregnancy:

- Thyroid hormone levels are dependent on the prevalence of thyroid autoantibodies in the population examined, which was not accounted for in the current model. Positive thyroid autoantibodies carry up to a 5-fold risk of hypothyroidism in geographic regions of iodine sufficiency (Moleti M et al; PMID 19179457).
- The accuracy of serum FT4 immunoassays in pregnancy has been questioned (Lee RH et al; PMID 19114271), due to their dependence on thyroid binding proteins.
- A recent review provides a comprehensive summary of this topic during pregnancy and should be included as a reference (Negro R et al; PMID 21247845).

Michael H. Lumpkin, Ph.D., DABT

The review of Moleti et al. (2011) cites 10 published studies of pregnant women in which threshold hypothyroxinemia was defined as the 2.5th or 10th percentile of fT4 in the respective cohort. As pointed out in the report, the fT4 levels represented in these percentiles are variable, likely being owed to cohort-specific fT4/TSH characteristics or differences in laboratory analytical capabilities brought to bear on each cohort's analysis of thyroid hormones. The normalization of study-specific thyroid hormone means for euthyroid and hypothyroid women is justified in order to use a single BBDR model to be used for dose-response analyses based on disparate data sets. The normalization procedure described in the report appropriately adjusts the "normal" and hypothyroxinemic ranges reported in the literature.

Elizabeth N. Pearce, M.D., M.Sc.

The existing literature regarding effects of maternal hypothyroxinemia in pregnancy variably uses thresholds of the 2.5th, 5th, or 10th percentile to define the condition. Therefore, I think this range is reasonable in pregnancy. A similar normalization approach for maternal thyroid function across different assay platforms has recently been described: Bestwick JP, John R, Maina A, Guaraldo V, Joomun M, Wald NJ, Lazarus JH. Thyroid stimulating hormone and free thyroxine in pregnancy: expressing concentrations as multiples of the median (MoMs). Clin Chim Acta. 2014;430:33-7.

There is currently no accepted clinical definition of isolated hypothyroxinemia outside of the pregnancy setting. In the absence of an accepted definition at these life stages, using the 2.5th to 10th percentile of the fT4 distribution is reasonable.

Stephen M. Roberts, Ph.D.

The SAB Perchlorate Advisory Panel noted the following in their report: "Perhaps most critical are the findings from studies examining the effects of isolated maternal hypothyroxinemia, defined as a free thyroxine (fT4) value in the lower end of the normal range with normal levels of TSH. This research has involved a variety of cutoffs to signify maternal hypothyroxinemia ranging from fT4 below the 10th or 5th percentiles to below the 2.5th percentile (Moleti et al. 2011), with the former percentiles being used to investigate neurodevelopmental outcomes and the latter the incidence and effects on pregnancy (e.g., Casey et al. 2005). Children exposed gestationally to maternal hypothyroxinemia (without hypothyroidism) show reduced levels of global and specific cognitive abilities, as well as increased rates of behavior problems including greater dysregulation in early infancy and attentional disorders in childhood (Man et al. 1991; Pop et al. 1999; Pop et al. 2003; Kooistra et al. 2006). Notably these effects are correlated with both degree (Pop et al. 1999; Henrichs et al. 2010) and duration (Pop et al. 2003) of maternal hypothyroxinemia. The Henrichs (2010) study, which stratified children into severe (<5th percentile) and mild (5-10th percentile) maternal hypothyroxinemia subgroups, showed that while effects were stronger and broader in the severe subgroup, the mild subgroup still showed delayed language development, thus suggesting that any factor that lowers maternal fT4, even slightly, can affect the offspring." (SAB 2013; pg. 10). The assumed range between the 2.5th and 10th percentile of the fT4 distribution is reasonable and consistent with the discussion presented by the SAB panel for pregnant women relative to risk to the fetus. However, as discussed in response to charge question 1C, modeling fetal thyroid hormone changes is unnecessary and problematic. Also, no rationale is presented for modeling fT4 in lactating women — they are not a sensitive life stage — and the relevance of determining an appropriate range for fT4 in these individuals is therefore unclear.

Understanding thyroid hormone changes in breast-fed and bottle-fed infants is important, but a clearer case needs to be made why the range between the 2.5th and 10th percentile of the fT4 distribution is appropriate. Are there empirical observations to support this range as associated with increased risk of impaired neurodevelopment in neonates and infants, or is it selected on another basis (e.g., as a matter of consistency with maternal hypothyroxinemia and risk to the fetus, or simply as a conservative choice)? Some discussion of the extent of diminished thyroid hormones in neonates and infants associated with neurological impairment (e.g., studies of transient hypothyroxinemia of prematurity and children with congenital hypothyroidism) might be helpful in providing perspective [Note: The SAB panel encouraged the EPA to examine this literature as part of an effort to better understand thyroid hormone disruption associated with adverse effects on neurodevelopment.]

Joanne F. Rovet, Ph.D.

I disagree with this reference range. Most studies (of mothers) use a value below the 5th percentile and when studies do examine mother-child pairs with maternal values up to the 10th percentiles, these are done in a correlational design with results showing no or very mild effects for offspring of mothers with mild (i.e., 5th to 10th percentile) hypothyroxinemia. I would also like to see effects of values below 2.5th percentile and the impact on subclinical or compensated hypothyroidism. It is not a given that TSH is elevated when fT4 is below the 2.5th percentile nor

not elevated when above this value. There are to my knowledge no reference levels for hypothyroxinemia in infants.

Note that I was one of the writers of the cited section of the SAB-PAP report. Rereading the section and recalling the discussion, it wasn't that these findings (i.e., hypothyroxinemia) were more critical than those on subclinical hypothyroidism; rather, these findings were relevant in that even a low fT4 with a normal TSH, particularly when the fT4 was below the 5th percentile, had consequences for later offspring outcome. In other words, this interpretation is taken out of context. Furthermore, the decision to exclude TSH seems to be based totally on an old (1981) paper by Silva and Silva, I believe from Chile, and this needs to be supported by more recent evidence.

Question 4B. Model predictions for zero intake of perchlorate indicate the range of iodine ingestion for which these life-stages are expected to be euthyroid vs. hypothyroxinemic. Are these predictions reasonable and have they been appropriately described and supported in the model and the report?

Hugh A. Barton, Ph.D.

This reviewer cannot comment on the range of iodine intake beyond noting that the descriptions in the report appeared clear.

Claude Emond, Ph.D.

The predictions and descriptions are appropriate to support the model.

Dale Hattis, Ph.D.

As far as I can tell at this stage, there is every expectation that some people in iodine deficient areas and elsewhere will be hypothyroxinemic at zero perchlorate exposure. This should be checked against actual NHANES data and juxtaposed with information on local water perchlorate levels in the areas where the NHANES subject resided.

Angela M. Leung, M.D., M.Sc.

Comments regarding the effects of zero perchlorate exposure and iodine ingestion on serum thyroid function:

Perchlorate exposure will invariably co-occur with other thyroid toxicants, many of which are similarly ubiquitous and also have inhibitory effects on iodine at NIS. The best well-described known examples are thiocyanate and nitrate, and their effects should be included in the model. As such, zero perchlorate exposure cannot necessarily be assumed to result in serum thyroid function changes resulting from iodine intake alone, but rather as a combined result from other coexposures and iodine intake. However, of these three known NIS inhibitors, perchlorate has been demonstrated to have the strongest effect in competitively inhibiting iodine uptake at NIS (Tonacchera et al; PMID 15650353).

Michael H. Lumpkin, Ph.D., DABT

The ranges of euthyroid (<100 µg/day) and hypothyroxinemic (75 µg/day or less) iodide intake levels for the BBDR model are appropriately described in the report. The report repeatedly warns of the uncertainty in model predictions of fT4 levels at iodide levels in the hypothyroxinemic range, as TSH-mediated regulation of iodide transport and T4 production are expected to be activated.

Elizabeth N. Pearce, M.D., M.Sc.

Figures depicting the dose-response curves for free T4 across perchlorate exposures are challenging to interpret as currently presented. However, it is noted on page 18 that at 75 mcg/day iodine ingestion pregnant and lactating women are assumed to be hypothyroid, and that at <100 mcg/day iodine intake the fT4 approaches the lower end of the maternal reference ranges even in the absence of perchlorate exposure. In reality, the literature demonstrates that at those iodine intakes there is a wide range of maternal thyroid function values, likely reflecting substantial intraindividual variations in adaptive capacity, and although median TSH might be higher in populations of pregnant or lactating women with iodine ingestion 75 mcg/L than in those with adequate iodine intakes, the vast majority of women likely would not be hypothyroid. It is for that reason, that serum TSH, free T4, and T3 are considered highly insensitive as biomarkers for population or individual iodine status in adults, including pregnant and lactating women (Pearce EN, Caldwell KL. Urinary iodine, thyroid function, and thyroglobulin as biomarkers of iodine status. Am J Clin Nutr. 2016;104 Suppl 3:898S-901S). This is, in part, which I think it is important to include the full HPT axis in the models.

For breastfed infants, if 75 mcg/day maternal iodine ingestion was assumed for pregnancy and maternal intake in lactation was <100 mcg/day, the model suggests that FT4 is low even in the absence of perchlorate exposure. This assumption may be overly conservative, but is reasonably well supported by data in the report.

Stephen M. Roberts, Ph.D.

Providing model predictions of fT4 levels with zero intake of perchlorate should provide an opportunity to check the accuracy of predictions, but unfortunately there are few studies relating iodine intake and fT4 levels in the life stages of interest. For example, the modeling predicts that a pregnant or lactating woman with 75 µg/d iodine intake and no perchlorate exposure will be hypothyroid. I found no study that indicates whether or not this prediction is plausible, and the report itself provides no discussion of the reasonableness of the estimates. So, while the predictions are described, they are not supported [as valid] in the report.

Joanne F. Rovet, Ph.D.

I don't understand the question. Hypothroxinemia in the 5-10% range is not to me a problem of concern for the developing infant. There are no data examining infant fT4 levels in this range and later outcome. Note: most concern for later outcome has generally reflected the maternal state throughout pregnancy and not the neonatal state in children who do not have congenital hypothyroidism. However, a recent study by C Trumpff et al. (2016, Frontiers in Endocrinology) that examined the relationship between elevated TSH levels at birth and preschool-age behavior problems in an area of mild iodine deficiency reported no association. Further, Oken et al. (2009, JCEM) studying the relationships between neonatal fT4 levels (all levels) and subsequent abilities reported an *inverse* relationship with visual recall at 6 months and no relationship with language or visuomotor development at age 3 years.

Question 4C. Based on the perchlorate level at which each life stage is predicted to become hypothyroxinemic (for a given iodine ingestion rate), it appears that the lactating mother is more sensitive than the breast-fed infant for PND 30-90. In part, this occurs because breast feeding reduces the iodide available for the maternal thyroid. Are these predictions reasonable and have these predictions been appropriately described and supported in the model and the report?

Hugh A. Barton, Ph.D.

This reviewer cannot comment on the reasonableness of these predictions, though they appear well described in the report. Perhaps part of evaluating the reasonableness is to ask what the implications of hypothyroxinemia are for the lactating mother versus the breast-fed infant. For the infant, the concern would be impacts on neurodevelopment. Is the issue for the lactating mother, a direct impact on her heath or a concern for inadequate levels of iodine and/or thyroid hormones in breast milk for the infant? If the former, then the lactating mother's sensitivity would be an endpoint to consider, but if it is the latter, then despite the apparently greater sensitivity of the mother, the direct predictions for the infant would seem more relevant.

Claude Emond, Ph.D.

The prediction of the model is reasonable based on the prediction presented in the report (see Figures 4, 5, 6, and 7). This is true for the mother and infant prediction during lactation or none. However, there is a lack of data, so we do not have enough information to qualify the risk for the fetus. The authors of this report expressed very well the limitation and applicability of this model (pages 16 to 22). Also, it seems that the influence of perchlorate, iodine or both exposure has a higher impact from exposure to perchlorate during breast feeding.

Dale Hattis, Ph.D.

This seems reasonable. However, it is best evaluated by drawing on the empirical information generated with the information assembled via my response to question 4B, separated by pregnant vs lactating women subgroups.

Angela M. Leung, M.D., M.Sc.

Comments regarding hypothyroxinemia in the lactating mother at PND 30-90:

- Breastfeeding does require a greater available iodine supply to the mother, and thus the U.S. Institute of Medicine recommends a slightly higher Recommended Dietary Allowance (RDA) of iodine during lactation then pregnancy (although the WHO/UNICEF/IGN just recommends an overall higher daily intake during both pregnancy and lactation, compared to the non-pregnant, non-lactating adult).
- Assuming that this is the primary mechanism for the increased vulnerability of the lactating mother, it should be anticipated that the prediction would also hold true for the entire postnatal duration studied in the model, which is not suggested. Thus, model calibration parameters may be still be inexact in the model's present form.

Michael H. Lumpkin, Ph.D., DABT

The conceptual reasoning given in the report that the lactating mother is more sensitive than the breast-fed infant because of additional iodide loss to the milk is biologically plausible. However, the report could include plots of simulations showing this relationship. For example, plasma iodide plotted against breast milk iodide levels across gestation, particularly at lower iodide intake rates, could illustrate this suggested phenomenon.

Elizabeth N. Pearce, M.D., M.Sc.

It is true that secretion of a significant amount of iodine into breast milk has the potential to make iodine unavailable for the lactating woman's own thyroid, a problem potentially exacerbated by the high dietary iodine requirements in lactation, as well as by perchlorate exposure. However, in thinking about populations sensitive to the effects of perchlorate, the concern with regard to lactating women does not pertain to their own hypothyroxinemia, but to the potential for inadequate supply of iodine in the breast milk, with potential adverse consequences for the thyroid hormone status and, ultimately, neurodevelopment of the breastfed infant. Therefore, as above, I think the concept of modeling maternal hypothyroxinemia in the lactating mother herself is somewhat flawed. It doesn't really make sense to describe the lactating mother as more sensitive to the effects of perchlorate than her breastfed infant at days 30-90 since transient maternal hypothyroxinemia over that time frame likely would not have long-term consequences for the mother, but could for the infant. Clinically, in the U.S. we do not see a higher-than-usual incidence of maternal hypothyroidism in lactation, (outside the setting of autoimmune postpartum thyroiditis), which does suggest to me that the model's predictions may not be correct. Calibrating the lactating women model against a more robust dataset may help to determine whether hypothyroxinemia is truly more likely to develop in lactating women than in their infants.

Stephen M. Roberts, Ph.D.

It is argued that the model result indicating that the lactating mother is more sensitive to hypothyroxinemia from perchlorate than her breast-fed infant is plausible because breast-feeding reduces iodine available for the maternal thyroid. This appears to be largely speculation. Appendix F includes a comparison of fT4 between lactating, pregnant, and "all other" women using data from NHANES. Although the fT4 levels in lactating women appear to be lower than "all other women", levels in pregnant women are even lower. I am not aware of any evidence from the literature that breastfeeding increases the risk of thyroid deficiency (even subclinical) and none is provided in the report. It is possible that this finding indicates a problem with the modeling of fT4 in the lactating mother, the breast-fed infant, or both.

Joanne F. Rovet, Ph.D.

I am not aware of any data to support this prediction. I am also not aware of any data comparing thyroid hormone levels of breast-feeding and formula-feeding mothers.

Question 5. Robustness of model predictions and sensitivity at lower perchlorate dose levels:
The dose-response predictions from the BBDR model predict levels of fT4 for:
a) The pregnant mother and fetus at GW40 (Fig. 10);
b) The formula-fed infant with fixed (Fig. 11, 7 and 30 day infants) and variable (Fig. 12, 7 through 90 day infants) iodine levels in their formula; and
c) The breast-fed infant as a function of maternal perchlorate exposures and iodine ingestion (Fig. 13, 7 through 90 day infants).

For each of these subgroups, please characterize the extent of uncertainty along the dose-response curve. In particular, is the level of uncertainty acceptable at lower dose levels of perchlorate (e.g., at or below 4 µg/kg/d) and higher levels of iodine intake (e.g., 150 µg/d) for each of these subgroups (left upper corner of the dose-response curves)? Should EPA assume that the model becomes more uncertain with rising perchlorate dose levels and declining iodine ingestion, i.e., as model predictions for fT4 approach and move through the range of hypothyroxinemia. (It should be noted that calibration of the iodide and thyroid hormone sub-models used data for populations with higher iodine intake and background exposure to perchlorate.)

Hugh A. Barton, Ph.D.

For formula-fed and breast-fed infants, there were some data on urinary perchlorate in the 1 – 10 µg/L range that appears to somewhat inform lower perchlorate intake levels though it is difficult to assess how well it constrains the dose-response behavior of the model. It seems likely that the models becomes more uncertain with higher perchlorate exposures that result in greater inhibition and lower iodine levels, which at some point become hypotheyroxinemia with elevated TSH that the model explicitly does not address.

Claude Emond, Ph.D.

These figures generated with the two PBPK models seem convincing that the models are sensitive enough inside of clinical range. However, they need now to be compared to the relevant exposure source of perchlorate in water.

Dale Hattis, Ph.D.

Again, I think these model predictions are best evaluated with empirical NHANES data separated into geographic categories by estimate levels of perchlorate in water. Because I am unconvinced by the calibration of the model as indicated earlier, I don't entirely trust the model predictions and have no basis to evaluate how much they are likely to be off.

Angela M. Leung, M.D., M.Sc.

Comments regarding model predictions and sensitivity at lower perchlorate levels in:
Figures 10-13 were reviewed with specific focus on the curves for lower perchlorate exposure and higher dietary iodine intake levels (left upper corner of the dose-response curves). In accordance with some of the public comments submitted thus far, it is reasonable to consider not including those which calibration for the iodine and thyroid hormone submodels were not performed for, given the non-linear interdependence of iodine status with thyroid function –a relationship which is further complicated with the exposure to varying NIS inhibitors, including perchlorate. It is reasonable to assume that the models may be more uncertain for these areas which have not been calibrated for in the report.

Michael H. Lumpkin, Ph.D., DABT

With the exception of the formula-fed infant life stage, the assumption that the model predictions of fT4 become more uncertain as perchlorate exposure increases and iodide intake decreases appears to hold, particularly for the pregnant mother, based on the increasing proportion of the dose-response curves that move below the normalized 2.5th percentile level.

Elizabeth N. Pearce, M.D., M.Sc.

I think it is reasonable to assume for all of the models that there is a higher degree of uncertainty at both lower iodine and higher perchlorate exposure levels. There is likely less uncertainty in the formula-fed infant model, given that only adequate iodine intakes are assumed.

Stephen M. Roberts, Ph.D.

The model is predicated on the absence of a compensatory response throughout the predicted range of fT4 levels. This assumption becomes more tenuous with lower predicted fT4 levels, thus uncertainty in the results increases. Public commenters have argued that compensatory responses may in fact occur even within the hypothyroxinemia range that is the focus of this model, and that this needs to be incorporated into the model. I have not seen a clear presentation of data to support this contention, but it is an issue that should be addressed directly one way or another in the presentation of the model.

Joanne F. Rovet, Ph.D.

a) First, what is GW40? – I assume it is parturition at 40-weeks gestation. Sorry, defined in figure caption, but should be listed in list of abbreviations. I found Figure 10 hard to interpret as the lines weren't clearly distinct from each other. I presume everything that is grey is bad and this includes most iodide exposures when perchlorate exceeds 11.7 pM. As I can't make sense of "uncertainties" from this graph (an assumed knowledge that I lack), I cannot comment. However, one doesn't need a model to know that low iodine compounded with high perchlorate is bad based on the literature and clever extrapolations of the epidemiologists on the SAB-PAP panel. My concern is the assumption that the 40-week gestation pregnant mother represents all

of pregnancy when we know that all thyroid hormones change during different trimesters of pregnancy and the impact of insufficiency in early pregnancy may be more serious than later.

b) My concern here is neglecting the measurement of perchlorate in the water used to make formula for older infants. Also, it is not clear to me why there is an impact at day 7 in formula-fed infants. Wouldn't any contribution from mother have vanished by this time in light of the Vulsma et al. (1989) study.

c) As I am having much difficulty understanding and seeing the essence of each graph, I cannot comment here.

Question 6. Empirical functions to predict thyroid hormone levels: The pregnancy model (but not the lactation/infant models) uses empirical functions to make urinary clearance of iodine and metabolic degradation of T3 dependent on the iodine ingestion level, in order to predict observed nonlinearity in the relationship between thyroid hormone levels and iodine intake. Does this use of empirical functions result in predicted outcomes or trends that are not plausible for serum thyroid hormones, particularly fT4?

Hugh A. Barton, Ph.D.

This reviewer cannot comment on whether the predictions for serum thyroid hormones are plausible.

Claude Emond, Ph.D.

Empirical function is a good alternative when we do not have more information about biological observations. During many situations, the model was described by using a table function that showed biological observations by using an empirical distribution. The result provides an approximation of the plausible observation of the parameters. During the simulation performed in the context of short exposure, such as 90 days, the result is acceptable. However, to simulate the impact of lifetime exposure, repetitive gestation, or acyclic lactation, I think it would be better to express variations of the parameters.

Dale Hattis, Ph.D.

I can't tell from the information I have available.

Angela M. Leung, M.D., M.Sc.

Comments regarding empirical functions in the pregnancy model:

The pregnancy model as reported in Lumen et al 2013 (including Tables 2 and 3 and their corresponding text) was reviewed in relation to this question. The functions used in the pregnancy model regarding the urinary iodine clearance and metabolic degradation of T3 are supported by the trimester-specific calibration parameters used. The predicted outcomes and trends for serum FT4 concentrations, as presented in the pregnancy model, are plausible and in line with those reported for the high perchlorate exposure ("Taltal") group in the Tellez R et al 2005 report.

Michael H. Lumpkin, Ph.D., DABT

The use of empirical relationships to describe urinary iodine clearance and T3 degradation does not, based on the model performance shown in the report, appear to result in implausible thyroid hormone levels.

Elizabeth N. Pearce, M.D., M.Sc.

Urinary clearance of iodine in pregnancy is largely a function of glomerular filtration rates since iodine is believed to be largely passively excreted at the kidney. The amount of ingested iodine will strongly influence the urinary iodine concentration, but not necessarily the fraction of plasma iodine which is renally excreted. Degradation of maternal T3 is strongly influenced by high levels of type 3 deiodinase in the placenta. I am not aware of data demonstrating that there are alterations in the placental DIO3 activity relative to differing iodine intakes. Therefore, although the empirical functions help to fit the model to observed data, they are not necessarily in line with currently understood physiology. The need to make these empiric adjustments to the model suggests data gaps which are worth exploring through future studies.

Stephen M. Roberts, Ph.D.

I will defer to other panel members on this charge question.

Joanne F. Rovet, Ph.D.

I cannot comment although the findings presented in the two Lumen et al. (2013, 2015) papers seem clearer and more robust to me than the current.

Question 7. Characterization of model predictions: The pregnancy and infant/lactation models were developed to specifically consider the range of iodine ingestion and thyroidal uptake where TSH is expected to stay in its normal range (i.e., they do not account for HPT feedback control). Do the models represent a reasonable effort to describe the relationships between iodine intake, perchlorate exposure and thyroid function? Are they sufficiently specific to predict perchlorate-induced changes in thyroid hormones in these life-stages over the range indicated? Please characterize the robustness, precision and sensitivity of the models for the ability to extrapolate changes in T4 associated with perchlorate exposures over the range from low exposures (less than 1 µg/kg/d) to higher levels which the model and analysis predict to be hypothyroxinemic.

Hugh A. Barton, Ph.D.

As noted in the general comments, this is a systems model of substantial complexity that appears to have been reasonably developed based upon available scientific information. Absent working with the models to develop a detailed understanding of their behavior, I would not try to comment on robustness, precision, or sensitivity for predictions.

Claude Emond, Ph.D.

The models represent a reasonable effort, and the authors have provided detailed descriptions; therefore, it was possible to do use the model by utilizing the current literature.

I believe these are good models (PBPK model women-fetus and women- infant) because they describe the major step of the mode of action of the hypothyroxinemic by using recent literature. I believe that this PBPK model reached the maximum of its potential based on the literature available and referenced and can be used along with the exposure observation inside the range it was established or limited. I believe that this model will further improve and become more sophisticated when more information about biological observations are included. We need to remember that a model is a simplification of biological observations. We will probably never be able to describe in the close future all of the biological mechanism processes implicated in hypothyroxinemic; however, this PBPK model can include the major pieces of limiting step in the sequential mode of action causing this effect. Here, in this model, only the effect of a supplement of iodine and the exposure of perchlorate are considered in inducing hypothyroidism; nevertheless, other physiological disturbances may also cause the issue. In addition, this model predicts the range specified by the authors. In the future, the PBPK models will need to be challenged to characterize exposure situation out of the range mentioned in the report, to gain a better understanding about the limitation of each parameter implicated in the PBPK model, and to study the impact of this model on the fetus. Specifically, the fetus might be sensitive to perchlorate, but there is not enough information to conduct a simulation like we did for infants and women.

Dale Hattis, Ph.D.

Without the improved model performance tests on calibration I have described earlier, I cannot quantitatively evaluate the accuracy of the model predictions. The modes are "sufficiently specific to predict perchlorate-induced changes in thyroid hormones in these lifestages". How accurate the predictions are is anyone's guess.

Angela M. Leung, M.D., M.Sc.

Comments regarding characterization of model predictions:

The current model and sub-models are based on the assumption that the range of perchlorate exposure doses and iodine intake levels studied would be autoregulated by the thyroid to compensate for these perturbations, and thus only serum thyroxine levels are decreased while serum TSH concentrations remain normal (i.e., hypothroxinemia is the primary endpoint). The model attempts to describe the relationships between iodine intake, perchlorate exposure, and serum thyroid function, but may be significantly influenced by the following major limitations, as has been described in greater detail in my previous comments:

- Serum thyroid hormone concentrations in pregnancy cannot be reliably extrapolated for lactation.
- Lack of serum thyroid autoantibody data, which may impact serum thyroid hormone concentrations and reference ranges.
- Variation in breastmilk iodine content in relation to recent dietary iodine ingestion.
- Calibration of the model for many crucial parameters (iodine and concentrations in breastmilk, maternal urine, and infant urine, and for infant serum thyroid function) was based on the study by Leung 2012, which did not examine women who were exclusively breastfeeding. Thus, the iodine nutrition provided to their infants was derived from a combination of both breastmilk and infant formula.
- The effects of likely coexposures from other NIS inhibitors on breastmilk and urinary iodine and perchlorate concentrations, and or infant serum thyroid function, are not addressed.

Michael H. Lumpkin, Ph.D., DABT

The model performance across the various represented life stages appears to be robust for low perchlorate exposures and iodide intake levels resulting in thyroid hormone levels above the 10^{th} percentiles for the reference ranges. Although the model is restricted to represent limited thyroid hormone homeostasis in isolation of HPT feedback mechanisms (and, possibly, compensatory corrections of iodide uptake and transport inhibition), it represents a plausible and technically justified approach to defining the perchlorate dose-response across a narrow exposure range. Given the model's isolation from the HPT feedback mechanisms, there may be increased uncertainty in the dose-response curves as they approach the hypothyroxinemia/hypothyroidism threshold, defined herein at the 2.5^{th} percentile of fT4 levels. It is doubtful that TSH expression occurs in an "all or nothing" response immediately at T4 levels below the 2.5^{th} percentile. An

informative analysis would be to add a multiplicative factor to the NIS transport parameters (Vmax and Km for various tissues) that adjusts the effect of NIS inhibition as T4 levels approach the hypothyroid condition. Using this simple approach, the effect of compensatory upregulation of NIS activity can be explored and evaluated as plausible or not. This evaluation may add strength to the model to be used for dose-response assessment for perchlorate exposures up to 20 µg/kg/d, or may suggest that BBDR modeling of perchlorate during pre- and postpartum life stage must include more robust HPT feedback mechanisms to accurately model the effect on the thyroid by perchlorate.

Elizabeth N. Pearce, M.D., M.Sc.

As noted above, I believe that the lack of consideration of the HPT axis in the BBDR model is a very substantial limitation of the model. Effects of NIS inhibition on free T4 cannot necessarily be fully understood without factoring in compensatory processes. In addition, effects of TSH on the T3:T4 ratio might have deleterious effects for fetal hypothyroxinemia which cannot be appreciated without inclusion of the HPT axis in models. I would strongly favor expanding models to include the HPT axis (recognizing that this does add a substantial degree of complexity).

I would also favor eliminating consideration of maternal hypothyroxinemia as a primary outcome for the lactating women. Lactating women would still need to be modeled in order to estimate the amounts of breast milk iodine and perchlorate exposure to inform the model of free T4 in breastfed infants.

I would recommend expanding the pregnancy model to include the first and second trimesters, the gestational ages for which there are currently epidemiologic data to demonstrating adverse developmental effects of maternal hypothyroxinemia.

I would recommend adding effects of concomitant exposures to other environmental NIS inhibitors.

I would expand the literature search and use new data to further validate the expanded models.

Stephen M. Roberts, Ph.D.

The models make a reasonable effort to focus on a range of fT4 levels that is of concern from the standpoint of potential neurodevelopmental effects, yet is not so low as to trigger increased TSH, which would complicate the modeling substantially. The models make a reasonable effort to describe the relationships between iodine intake, perchlorate exposure and thyroid function for the sensitive life stages of interest. The last portion of the charge question appears to be similar to the question posed in 3C, except focuses specifically on the T4 predictions. The response is the same — the robustness, precision, and sensitivity are difficult to gauge based upon the information presented in the report. In part, this is due to the nature of the limited data available for external validation of the model predictions.

Joanne F. Rovet, Ph.D.

I am not sure why HPT feedback control is not considered when TSH is to me a marker of brain sufficiency of thyroid hormone. Thus, I am less than enthusiastic of the quality of the current models for predicting T4 changes following the various perchlorate exposures. Figure 17, however, shows the importance of iodide sufficiency.

V. SPECIFIC OBSERVATIONS ON MODEL REPORT

Hugh A. Barton, Ph.D.

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
12	1-2	Is the wording here, "particularly sensitive" "strongly supported" too strong.
23	15-17	As noted in comments above, clarify this sentence about halting the review process.
24	8	Change "where" to "were"
33	10	Hematocrit is referred to here and several additional times, but the values used do not appear to be reported.
85		In Figures and Tables or report and appendix, some parameters have _SENS added to their names, but it wasn't entirely clear what this meant, e.g., why do some parameters have it and other don't?

Claude Emond, Ph.D.

No specific observations on Model Report provided.

Dale Hattis, Ph.D.

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
--	--	**List of Abstracts of Papers that May Be Helpful in Quantitatively Estimating the Effects of Iodine and Thyroid Hormone Deficiency on IQ from Exposure During Early Pregnancy** **1. Morreale de Escobar G, Obregón MJ, Escobar del Rey F. Is Neuropsychological Development Related to Maternal Hypothyroidism or to Maternal Hypothyroxinemia? J. Clinical Endocrinology and Metabolism 85: 3975-3987.** **Abstract** Several recent publications have drawn attention to the role of the thyroid hormone status of the mother on the future neuropsychological development of the child. The screening of pregnant women for clinical or subclinical hypothyroidism based on second trimester elevated maternal TSH values has been proposed. **Here, we have summarized present epidemiological and experimental evidence strongly suggesting that conditions resulting in first trimester hypothyroxinemia (a low for gestational age circulating maternal free T_4, whether or not TSH is increased) pose an increased risk for poor neuropsychological development of the fetus.** This would be a consequence of decreased availability of maternal T_4 to the developing brain, its only source of thyroid hormone during the first trimester; T_4 is the

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
		required substrate for the ontogenically regulated generation of T_3 in the amounts needed for optimal development in different brain structures, both temporally and spatially. Normal maternal T_3 concentrations do not seem to prevent the potential damage of a low supply of T_4, although they might prevent an increase in circulating TSH and detection of the hypothyroxinemia if only TSH is measured. Hypothyroxinemia seems to be much more frequent in pregnant women than either clinical or subclinical hypothyroidism and autoimmune thyroid disease, especially in regions where the iodine intake of the pregnant woman is inadequate to meet her increased needs for T_4. It is proposed that the screening of pregnant women for thyroid disorders should include the determination of free T_4 as soon as possible during the first trimester as a major test, because hypothyroxinemia has been related to poor developmental outcome, irrespective of the presence of high titers of thyroid autoantibodies or elevated serum TSH. The frequency with which this may occur is probably 150 times or more that of congenital hypothyroidism, for which successful screening programs have been instituted in many countries. - See more at: [HYPERLINK "http://press.endocrine.org/doi/abs/10.1210/jcem.85.11.6961" \l "sthash.MBJebpGn.dpuf"] **2. Cao XY, Jiang XM, Dou ZH, Rakeman MA, Zhang ML, O'Donnel K, Ma T, Amette K, DeLong N, Delong GR. Timing of vulnerability of the brain to iodine deficiency in endemic cretinism. N Engl J Med. 1994 Dec 29;331(26):1739-44.** **Abstract** **BACKGROUND:** Endemic cretinism, caused by severe iodine deficiency during pregnancy, is the world's most common preventable cause of mental retardation. It can be prevented by iodine treatment before conception, but whether it can be prevented or ameliorated by treatment during pregnancy or after delivery is not known. **METHODS:** In a severely iodine-deficient area of the Xinjiang region of China, we systematically administered iodine to groups of children from birth to three years of age (n = 689) and women at each trimester of pregnancy (n = 295); we then followed the treated children and the babies born to the treated women for two years. We used three independent measures of neural development: the results of the neurologic examination, the head circumference (which correlates with brain weight in the first postnatal year), and indexes of cognitive and motor development. Untreated children one to three years of age, who were studied when first seen, served as control subjects.

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
		RESULTS: The prevalence of moderate or severe neurologic abnormalities among the 120 infants whose mothers received iodine in the first or second trimester was 2 percent, as compared with 9 percent among the 752 infants who received iodine during the third trimester (through the treatment of their mothers) or after birth (P = 0.008). The prevalence of microcephaly (defined as a head circumference more than 3 SD below U.S. norms) decreased from 27 percent in the untreated children to 11 percent in the treated children (P = 0.006), and the mean (+/- SD) developmental quotient at two years of age increased (90 +/- 14, vs. 75 +/- 18 in the untreated children; P < 0.001). Treatment in the third trimester of pregnancy or after delivery did not improve neurologic status, but head growth and developmental quotients improved slightly. Treatment during the first trimester, which was technically problematic, improved the neurologic outcome. **CONCLUSIONS:** Up to the end of the second trimester, iodine treatment protects the fetal brain from the effects of iodine deficiency. Treatment later in pregnancy or after delivery may improve brain growth and developmental achievement slightly, but it does not improve neurologic status. **Comment in** [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/7984200"] [N Engl J Med. 1994] 3. **Gilbert M, Rovet J, Chen Z, Koibuchi N.** [HYPERLINK "http://www.sciencedirect.com/science/article/pii/S0161813X11002051"], **Neurotoxicology, Volume 33 (2012) 842-852.** **Abstract** Thyroid hormones (TH) are critical for growth and development and particularly brain development. There are numerous environmental agents that lead to marginal reductions of circulating TH. Although it is clear that severe developmental hypothyroidism is profoundly detrimental to neurodevelopment, there is less information regarding the consequences of modest degrees of thyroid. The impact of low level TH disruptions induced by environmental contaminants has not been defined. This paper is a synopsis from four invited speakers who presented at the 13th International Neurotoxicology Association meeting held in Xi'an, China during the summer of 2011. An overview of the role of TH in brain development and a review of human and animal data on the neurological sequelae of disruption of the thyroid axis in the pre- and early post-natal periods were presented by Mary Gilbert and Joanne Rovet. Iodine deficiency, a common cause of TH

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
		insufficiency and mental retardation in many countries, including China, was addressed by Zupei Chen. In this presentation the current incidence of iodine deficiency and neurological outcome in China and the efficacy of recently implemented iodinization programs to eliminate this cause of mental retardation were reviewed. Joanne Rovet described the impact of TH disruption during pregnancy and under conditions of congenital hypothyroidism. Children born with normal thyroid function, but who experienced TH insufficiency in the womb, display subtle cognitive impairments and abnormalities in brain imaging. Despite early detection and treatment, deficiencies also exist in children born with thyroid disorders. Different patterns of cognitive effects result from prenatal versus postnatal TH insufficiency. Mary Gilbert reported on the effects of environmental contaminants with thyroid disrupting action on brain development in animals. Results of neurophysiological, behavioral, structural and molecular alterations that accompany modest perturbations of the thyroid axis were reviewed. Noriyuki Koibuchi described molecular targets of TH-mediated signaling accompanying exposure to persistent organic pollutants. Both polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) are prevalent environmental contaminants that disrupt TH signaling at the receptor level. This action by these chemical classes could contribute to the negative impact of these chemicals on brain function. In summary, epidemiological, preclinical and animal research has clearly identified the critical role of TH in brain development. Additional work is required to understand the impact of low level perturbations of the thyroid axis to evaluate the risk associated with environmental contaminants with thyroid action. 4. [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Taylor%20PN%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Okosieme%20OE%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Murphy%20R%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Hales%20C%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Chiusano%20E%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Maina%20A%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Joomun%20M%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Bestwick%20JP%5B

Specific Observations on Model Report		
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		Author%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Smyth%20P%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Paradice%20R%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Channon%20S%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Braverman%20LE%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Dayan%20CM%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Lazarus%20JH%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Pearce%20EN%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"]. **Maternal perchlorate levels in women with borderline thyroid function during pregnancy and the cognitive development of their offspring: data from the Controlled Antenatal Thyroid Study. **J Clin Endocrinol Metab. 2014 Nov;99(11):4291-8. doi: 10.1210/jc.2014-1901. Epub 2014 Jul 24.** **Abstract** **OBJECTIVE:** Thyroid dysfunction is associated with impaired cognitive development. Perchlorate decreases thyroidal iodine uptake, potentially reducing thyroid hormone production. It is unclear whether perchlorate exposure in early life affects neurodevelopment. **DESIGN:** Historical cohort analysis. **PATIENTS:** From 2002 to 2006, 21,846 women at gestational age <16 weeks recruited from antenatal clinics in Cardiff, UK and Turin, Italy were enrolled in the Controlled Antenatal Thyroid Screening Study (CATS). We undertook a retrospective analysis of 487 mother-child pairs in mothers who were hypothyroid/hypothyroxinemic during pregnancy and analyzed whether first trimester maternal perchlorate levels in the highest 10% of the study population were associated with increased odds of offspring IQ being in the lowest 10% at 3 years of age. **MAIN OUTCOME MEASURES:**

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
		Maternal urinary perchlorate, offspring IQ. **RESULTS:** Urine perchlorate was detectable in all women (median 2.58 μg/L); iodine levels were low (median 72 μg/L). **Maternal perchlorate levels in the highest 10% of the population increased the odds of offspring IQ being in the lowest 10% OR = 3.14 (95% CI 1.38, 7.13) P = .006 with a greater negative impact observed on verbal OR = 3.14 (95% CI 1.42, 6.90) P = .005 than performance IQ. Maternal levothyroxine therapy did not reduce the negative impact of perchlorate on offspring IQ.** **CONCLUSIONS:** This is the first study using individual-level patient data to study maternal perchlorate exposure and offspring neurodevelopment and suggests that high-end maternal perchlorate levels in hypothyroid/hypothyroxinemic pregnant women have an adverse effect on offspring cognitive development, not affected by maternal levothyroxine therapy. These results require replication in additional studies, including in the euthyroid population. **Comment in** • [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/25372124"] [J Clin Endocrinol Metab. 2014] PMID: 25057878 DOI: [HYPERLINK "https://dx.doi.org/10.1210/jc.2014-1901"][PubMed - indexed for MEDLINE] 5. **Lain, SJ, Bentley, JP, Wiley, V, Roberts, CL, Jack, M, Wilcken, B., Nassar, N. Association between borderline neonatal thyroid-stimulating hormone concentrations and educational and developmental outcomes: a population-based record-linkage study.** [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=association+between+borderline+neonatal+thyroid-stimulating+hormone+concentrations+and+educational" \o "The lancet. Diabetes & endocrinology."] **2016 Sep;4(9):756-65. doi: 10.1016/S2213-8587(16)30122-X. Epub 2016 Jul 22.** **Summary** **Background** Congenital hypothyroidism causes intellectual delay unless identified and effectively treated soon after birth. Newborn screening has almost eliminated intellectual disability associated with congenital hypothyroidism. However, clinical uncertainty remains about infants with thyroid-stimulating hormone

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
		(TSH) concentrations less than the newborn screening cutoffs. We assessed the association between neonatal TSH concentrations and educational and developmental outcomes. **Methods** We did a population-based record-linkage study of all liveborn infants undergoing newborn screening from 1994 to 2008 in New South Wales, Australia, with assessments of childhood development or school performance. Very-low-birthweight babies (<1500 g) were excluded. Developmental and educational outcomes were obtained and these were linked to individual records by the New South Wales Centre for Health Record Linkage. The primary educational outcome was the proportion of students with National Assessment Program Literacy and Numeracy (NAPLAN) results lower than the national minimum standard in reading or numeracy measured at all ages, and the primary developmental outcome was the proportion of children who were classified as being developmentally high risk (vulnerable in two or more of the five developmental domains assessed by the Australian Early Development Census) at age 4–6 years. The proportions of infants with each outcome were calculated per percentile (0–100) of TSH concentration. Multivariable logistic regression was used to account for potential confounding by maternal and fetal variables known to affect neonatal TSH concentrations or neurodevelopmental outcomes. **Findings** 503 706 infants had a neonatal TSH result that linked to a developmental or educational outcome. 149 569 infants born between 2002 and 2008 were linked to an Australian Early Development Census developmental outcome and 354 137 were linked to a NAPLAN educational outcome. Median follow-up for educational outcome was 10 years (IQR 8–12) and for developmental outcome was 5 years (5–6). 5·5% (14 137 of 257 752) of infants with TSH concentrations lower than the 75th percentile scored less than the national minimum standard for numeracy, and this increased with each increase of percentile group to 11·3% (15 of 133) of infants with a TSH concentration between the 99·90th and 99·95th percentile. Infants with a neonatal TSH concentration in the 99·95th percentile or higher (above newborn screening cutoff) and likely to have diagnosed and treated congenital hypothyroidism had similar results to infants with a TSH concentration lower than the 75th percentile for both educational and developmental outcomes. Infants with a neonatal TSH concentration between the 99·5th and 99·9th percentile were more likely to have special needs (adjusted odds ratio [aOR] 1·68, 95% CI 1·23–2·30), poor numeracy performance (aOR 1·57, 1·29–1·90), and developmentally high risk (aOR 1·52, 1·20–1·93).

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
		Interpretation We found an association between neonatal TSH concentrations lower than the present newborn screening thresholds and poor educational and developmental outcomes. This association needs further investigation to assess whether assessment and treatment of these infants might improve their long-term cognitive outcomes. **Funding** Australian National Health and Medical Research Council. 6. **Bath SC, Steer CD, Golding J, Emmett P, Rayman MP. Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC), Lancet. 2013 Jul 27;382(9889):331-7. doi: 10.1016/S0140-6736(13)60436-5. Epub 2013 May 22.** **Summary** **Background: As a component of thyroid hormones, iodine is essential for fetal brain development. Although the UK has long been considered iodine replete, increasing evidence suggests that it might now be mildly iodine deficient. We assessed whether mild iodine deficiency during early pregnancy was associated with an adverse effect on child cognitive development.** **Methods: We analysed mother–child pairs from the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort by measuring urinary iodine concentration (and creatinine to correct for urine volume) in stored samples from 1040 first-trimester pregnant women. We selected women on the basis of a singleton pregnancy and availability of both a urine sample from the first trimester (defined as ≤13 weeks' gestation; median 10 weeks [IQR 9–12]) and a measure of intelligence quotient (IQ) in the offspring at age 8 years. Women's results for iodine-to-creatinine ratio were dichotomised to less than 150 µg/g or 150 µg/g or more on the basis of WHO criteria for iodine deficiency or sufficiency in pregnancy. We assessed the association between maternal iodine status and child IQ at age 8 years and reading ability at age 9 years. We included 21 socioeconomic, parental, and child factors as confounders.** **Findings: The group was classified as having mild-to-moderate iodine deficiency on the basis of a median urinary iodine concentration of 91·1 µg/L (IQR 53·8–143; iodine-to-creatinine ratio 110 µg/g, IQR 74–170). After adjustment for confounders, children of women with an iodine-to-creatinine ratio of less than 150 µg/g were more likely to have scores in**

Specific Observations on Model Report		
Page	*Line*	*Comment or Question*
		the lowest quartile for verbal IQ (odds ratio 1·58, 95% CI 1·09–2·30; p=0·02), reading accuracy (1·69, 1·15–2·49; p=0·007), and reading comprehension (1·54, 1·06–2·23; p=0·02) than were those of mothers with ratios of 150 µg/g or more. When the less than 150 µg/g group was subdivided, scores worsened ongoing from 150 µg/g or more, to 50–150 µg/g, to less than 50 µg/g. **Interpretation: Our results show the importance of adequate iodine status during early gestation and emphasize the risk that iodine deficiency can pose to the developing infant, even in a country classified as only mildly iodine deficient. Iodine deficiency in pregnant women in the UK should be treated as an important public health issue that needs attention.** **7. Min H, Dong J, Wang Y. et al. Maternal Hypothyroxinemia-Induced Neurodevelopmental Impairments in the Progeny. Molecular Neurobiology 53(3): 1613-1624.** **Abstract** Maternal hypothyroxinemia can induce neurodevelopmental impairments in the developing fetus. We here review recent studies on the epidemiology and molecular mechanisms associated with this important public health issue. In 2011, the American Thyroid Association defined maternal hypothyroxinemia as low serum free thyroxine (FT4) levels (<5th or <10th percentile) existing in conjunction with normal serum free triiodothyronine (FT3) or thyroid stimulating hormone (TSH) levels during pregnancy. Compared to clinical or subclinical hypothyroidism, hypothyroxinemia is more commonly found in pregnant women. Hypothyroxinemia usually ensues in response to several factors, such as mild iodine deficiency, environmental endocrine disrupters, or certain thyroid diseases. Unequivocal evidence demonstrates that maternal hypothyroxinemia leads to negative effects on fetal brain development, increasing the risks for cognitive deficits and poor psychomotor development in resulting progeny. In support of this, rodent models provide direct evidence of neurodevelopmental damage induced by maternal hypothyroxinemia, including dendritic and axonal growth limitation, neural abnormal location, and synaptic function alteration. The neurodevelopmental impairments induced by hypothyroxinemia suggest an independent role of T4. Increasing evidence indicates that adequate thyroxine is required for the mothers in order to protect against the abnormal brain development in their progeny. **8. Korevaar TI, Muetzel R, Medici M, Chaker L, Jaddoe, VWV, B de Rijke, Y, Steegers, EA, Visser TJ, White T, Tiemeier H, Peeters RP. Association of maternal thyroid function during**

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
		early pregnancy with off spring IQ and brain morphology in childhood: a population-based prospective cohort study. The Lancet Diabetes-Endocrinology 2016 4:35-43. **Background** Thyroid hormone is involved in the regulation of early brain development. Since the fetal thyroid gland is not fully functional until week 18–20 of pregnancy, neuronal migration and other crucial early stages of intrauterine brain development largely depend on the supply of maternal thyroid hormone. Current clinical practice mostly focuses on preventing the negative consequences of low thyroid hormone concentrations, but data from animal studies have shown that both low and high concentrations of thyroid hormone have negative effects on offspring brain development. We aimed to investigate the association of maternal thyroid function with child intelligence quotient (IQ) and brain morphology. **Methods** In this population-based prospective cohort study, embedded within the Generation R Study (Rotterdam, Netherlands), we investigated the association of maternal thyroid function with child IQ (assessed by non-verbal intelligence tests) and brain morphology (assessed on brain MRI scans). Eligible women were those living in the study area at their delivery date, which had to be between April 1, 2002, and Jan 1, 2006. For this study, women with available serum samples who presented in early pregnancy (<18 weeks) were included. Data for maternal thyroid-stimulating hormone, free thyroxine, thyroid peroxidase antibodies (at weeks 9–18 of pregnancy), and child IQ (assessed at a median of 6·0 years of age [95% range 5·6–7·9 years]) or brain MRI scans (done at a median of 8·0 years of age [6·2–10·0]) were obtained. Analyses were adjusted for potential confounders including concentrations of human chorionic gonadotropin and child thyroid-stimulating hormone and free thyroxine. **Findings** Data for child IQ were available for 3839 mother–child pairs, and MRI scans were available from 646 children. Maternal free thyroxine concentrations showed an inverted U-shaped association with child IQ (p=0·0044), child grey matter volume (p=0·0062), and cortex volume (p=0·0011). For both low and high maternal free thyroxine concentrations, this association corresponded to a 1·4–3·8 points reduction in mean child IQ. Maternal thyroid stimulating hormone was not associated with child IQ or brain morphology. All associations remained similar after the exclusion of women with overt hypothyroidism and overt hyperthyroidism, and after adjustment for concentrations of human chorionic gonadotropin, child thyroid-

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
		stimulating hormone and free thyroxine or thyroid peroxidase antibodies (continuous or positivity). **Interpretation** Both low and high maternal free thyroxine concentrations during pregnancy were associated with lower child IQ and lower grey matter and cortex volume. The association between high maternal free thyroxine and low child IQ suggests that levothyroxine therapy during pregnancy, which is often initiated in women with subclinical hypothyroidism during pregnancy, might carry the potential risk of adverse child neurodevelopment outcomes when the aim of treatment is to achieve high-normal thyroid function test results. **9.** [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Taylor%20PN%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Okosieme%20OE%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Murphy%20R%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Hales%20C%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Chiusano%20E%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Maina%20A%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Joomun%20M%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Bestwick%20JP%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Smyth%20P%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Paradice%20R%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Channon%20S%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Braverman%20LE%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Dayan%20CM%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK "https://www.ncbi.nlm.nih.gov/pubmed/?term=Lazarus%20JH%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"], [HYPERLINK

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
		"https://www.ncbi.nlm.nih.gov/pubmed/?term=Pearce%20EN%5BAuthor%5D&cauthor=true&cauthor_uid=25057878"]. **Maternal perchlorate levels in women with borderline thyroid function during pregnancy and the cognitive development of their offspring: data from the Controlled Antenatal Thyroid Study. J Clin Endocrinol Metab 2014 Nov;99(11):4291-8. doi: 10.1210/jc.2014-1901. Epub 2014 Jul 24.** **Objective:** Thyroid dysfunction is associated with impaired cognitive development. Perchlorate decreases thyroidal iodine uptake, potentially reducing thyroid hormone production. It is unclear whether perchlorate exposure in early life affects neurodevelopment. **Design:** Historical cohort analysis. **Patients:** From 2002 to 2006, 21,846 women at gestational age <16 weeks recruited from antenatal clinics in Cardiff, UK and Turin, Italy were enrolled in the Controlled Antenatal Thyroid Screening Study (CATS). We undertook a retrospective analysis of 487 mother-child pairs in mothers who were hypothyroid/hypothyroxinemic during pregnancy and analyzed whether first trimester maternal perchlorate levels in the highest 10% of the study population were associated with increased odds of offspring IQ being in the lowest 10% at 3 years of age. Main Outcome Measures: Maternal urinary perchlorate, offspring IQ. **Results:** Urine perchlorate was detectable in all women (median 2.58 µg/L); iodine levels were low (median 72 µg/L). Maternal perchlorate levels in the highest 10% of the population increased the odds of offspring IQ being in the lowest 10% OR=3.14 (95% CI 1.38, 7.13) P=.006 with a greater negative impact observed on verbal OR=3.14 (95% CI 1.42, 6.90) P=.005 than performance IQ. Maternal levothyroxine therapy did not reduce the negative impact of perchlorate on offspring IQ. **Conclusions:** This is the first study using individual-level patient data to study maternal perchlorate exposure and offspring neurodevelopment and suggests that high-end maternal perchlorate levels in hypothyroid/hypothyroxinemic pregnant women have an adverse effect on offspring cognitive development, not affected by maternal levothyroxine therapy. These results require replication in additional studies, including in the euthyroid population. (J ClinEndocrinolMetab 99: 4291–4298, 2014)
6	5-16	This risks missing possibly the most serious effects on IQ for pregnant women in the lowest range of iodide intake. This may not control RfD selection, but may well be very important for estimating overall IQ effects

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
		and therefore juxtaposing costs and benefits of alternative choices of RfDs and measures to reduce perchlorate exposures.
6	18-21	Could be a substantial limitation.
7	2-8	Critically evaluate this evidence supporting model calibration.
7	9-16	These ranges of iodide intake seem unduly restricted—support with reference to actual US iodide intake and excretion information from NHANES.
7	17-25	Having "reference intervals" as the touchstone of the analysis is distinctly suboptimal for juxtaposing relative costs and benefits of regulatory options. Much better would be to make predictions of IQ effects which can be economically valued and juxtaposed with estimates of economic costs.
7	26-32 33-36 Footnote 2	What? No analysis of variability and uncertainty in this parameter (refers to "the revised value" implying no distributional treatment for what is stated to be a key component of the analysis). Variability—why is it assumed that everyone is the same in this? Uncertainty—surely the value has not been determined to a precision where the implications of uncertainty need not be analyzed.
8	15-20	Analysis by "reference range" is likely to be misguided. Changes within the reference range may still be associated with harm. This focus on reference ranges and the lack of data for potentially the most vulnerable segment of the population is an additional reason to treat the modeling results with considerable caution in judging appropriate exposure control standards.
9	6-13	This clearly requires quantitative assessment of the effects of exposure changes for the entire population, not just the segments for which a "reference range" is available. The effects of interest include prominently those on IQ, for which it would be possible to juxtapose quantifiable economic benefits with quantifiable economic costs. And the analysis must clearly include the full range of iodine intakes in the real US population, as best it can be estimated from available data.

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
11	1-13	These references must be systematically evaluated in order to convert the analysis to implications for IQ changes rather than just "hypothyroxemia." Such conversion is essential for a reasonable juxtaposition of costs and benefits of regulatory alternatives. The abstract for the most recent Min et al. (2016) is: [HYPERLINK "http://link.springer.com/journal/12035"] April 2016, Volume 53, [HYPERLINK "http://link.springer.com/journal/12035/53/3/page/1"], pp 1613–1624 Maternal Hypothyroxinemia-Induced Neurodevelopmental Impairments in the Progeny • Authors Authors and affiliations • Hui Min, Jing Dong, Yi Wang, Yuan Wang, Weiping Teng, Qi Xi. 2016. • Hui Min1 2 • Jing Dong 12 • Yi Wang1 2 • Yuan Wan g12 • Weiping Teng2 • Qi Xi3 [HYPERLINK "mailto:cmuqixi @hotmail.com"] • Jie Chen1 2 [HYPERLINK "mailto:chenjie@ mail.cmu.edu.cn"] 1. Department of Occupational and Environmental Health, School of Public HealthChina Medical UniversityShenyangPeople's Republic of China 2. Liaoning Provincial Key Laboratory of Endocrine DiseasesThe First Hospital of China Medical UniversityShenyangPeople's Republic of China 3. Department of PhysiologyThe University of Tennessee Health Science CenterMemphisUSA Article **First Online:** 11 February 2015 **DOI**: 10.1007/s12035-015-9101-x **Cite this article as:**
12-13	--	Need to add to Schlosser document reference to biphasic relationship between fT4 during pregnancy and childhood nonverbal IQ measures and

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
		brain size measures. This would allow reframing of measures of TH perturbation to measures of IQ directly relatable to serious economic and other consequences as a function of iodide intake distributions.
14	--	Model should clearly be extended to cover effects during early pregnancy where T4 deficiency is likely to have the greatest effects on neurodevelopment.
16	footnote	[3] Here we use "reference range" to refer to the range of a hormone that is considered normal and healthy for a population. Hence some in the population will have hormone levels above or below that reference range and be identified as having an adverse clinical condition. The "population distribution" refers to the distribution of hormone levels in the entire population, including those outside of the reference range. [4] The model does not describe TSH levels, but assumes they stay within the normal reference range. Clinically, significant elevations in TSH can be observed whether or not T4 of fT4 are in the reference range. Thus there are not specific levels of T4/fT4 that are definitively associated with TSH elevation. This may be due to inter-individual variability in hormonal control mechanisms. But mechanistically it is known that TSH production and release are stimulated by decreasing T4 levels. Hence for the purpose of this model, specific, life-stage-specific fT4 levels are identified below which TSH levels are expected to be sufficiently stimulated as to rise above their reference range and introduce significant feedback control on the thyroid, which would make model predictions invalid.
17	12-21	There is no apparent justification for drawing the line at the 2.5th percentile. This is pretty important because it may be that later the authors essentially ignore possible effects outside this limit, thus potentially biasing the analysis by excluding an especially sensitive segment of the population.
17	22-24	I think this is a problem for the analysis—levels of iodide intake below this are present in the US population (analyze NHANES data) and likely represent a sensitive subgroup that could affect expected IQ benefits of perchlorate exposure reduction.
18	2-13	
18	14-25	There is a grave danger here of understating perchlorate hazard and benefits of exposure reduction. The analysis should consider the effects of perchlorate for the full range and frequency of iodide exposures in the U.S. population. Otherwise both the baseline amount of harm from current perchlorate exposures and the benefits and costs of changes in those exposures will be mis-analyzed. (give fuller analysis of this distribution here?)
20	8-15	More explanation is needed for the choice of this distribution. Why not use a lognormal? Data should be shown to indicate that a normal or lognormal does not fit, if that is true. See analysis of the data in App-25 below.
44	22-24	

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
45	1-23	The single-value for this binding constant has been changed more than 2-fold from the earlier value. Yet there is no allowance for either variability or uncertainty. This should be improved in subsequent analyses to at least provide some sensitivity analysis for both uncertainty and variability. Analyze in detail.
45	9-16	Overall this conclusory presentation leaves much to be desired. Comparisons to the data fits before and after revision should be provided to allow a meaningful review.
45	17-23	This certainly suggests that something may be amiss in the basic calibration of the model. It is reassuring that the author does not think that key predictions in the current analysis are not affected much, but because other uses of the model are expected in the future, this issue may well need to be revisited.
46	2-12	
60	10-19	This is completely unconvincing. The figure referred to has an enormous amount of scatter, even with the data points plotted on a logarithmic y-axis. To then say, given this scatter, that "the model-predicted urinary iodide concentrations…were within the range of literature-reported values (Figure 4) really is such a loose standard that it seems hardly meaningful. Minimally, there needs to be some statistical summarization of the comparison data and some specific comparison of the summary data with a specific set of model predictions.
61	6-12	The comparison depicted in the bottom panel is also unconvincing, lacking any statistical summarization to help the reader judge whether the comparison supports or refutes the predictions of the model.
63	10-17	Similarly, the conclusion from Figure 6 that the predicted perchlorate concentrations are "within the range of reported values" is completely unconvincing. What is shown in Figure 6 is a plot of highly scattered observations plotted over a four order of magnitude range with no statistical summarization of the data to allow reasonable juxtaposition of the central tendency and uncertainty range of the observations with corresponding model expectations.
64	9-13	The lack of correspondence of the data points to model predictions is unsettling. And the proffered explanation "that iodide levels are not stable in breast-milk samples" is no help. Instability would be expected to lead to scatter of the data points, but not a systematic bias lowering the data points relative to model expectations. The modelers' response in this case makes no sense.
67	11-12	As indicated by my remarks above, I disagree. The authors should develop a range of alternative models that would fit these data as well or better based on much more rigorous criteria than that the models produce results "within the range" of the observations presented on multi-order-of magnitude plots. They should then document the implications of the alternative models for the

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
		effect of various levels of perchlorate on range of policy-relevant parameter values such as IQ distributions.
69	7-12	Although the authors seem to be following SAB advice in this choice of criteria for defining adversity, I think it would be much better to use-IQ change criteria based on recently available information. Making IQ change the focus of the analysis can build upon the modeling work done so far, but yield results in terms that can be valued economically and juxtaposed much more readily with costs of alternative measures to reduce perchlorate exposures. This corresponds much more closely to the mandate for analysis under the Safe Drinking Water Act, as I understand it and described in the introductory sections of the model report.
70	11-14	There should be an analysis of the effects of a plausible uncertainty range for this parameter, given that it has been appreciably changed from what was assumed in prior modeling. The authors may also wish to explore the potential consequences of variability among people in the values of this key parameter, particularly if a literature search yields evidence of a polymorphism in the gene related to this binding constant. At the very least, there should be some discussion of the possibility that this gene may be polymorphic.
71	3-6	Surely the model results are uncertain both above and below the indicated level. Perhaps they are more uncertain below 10.6 ppm but the criterion indicated cannot indicate a sharp cutoff where uncertainty starts.

Angela M. Leung, M.D., M.Sc.

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
Throug hout	--	Suggest replacing the term "bottle-fed" with "formula-fed" throughout the report and its figures. Currently, both are used interchangeably, and thus it should be clarified that the contents of the infant bottle are referring to only infant formula, rather than breastmilk or a combination of both.
8	10	Suggest deleting "medically"
16	Footnote 4	• Suggest clarifying the first sentence by inserting "serum" before TSH. • The second sentence would be better rephrased by deleting the word "Clinically". • There is typo in the second sentence: "T4 or FT4" levels The 4th and 5th sentences should be combined and can be better rephrased as: "This may be due to inter-individual variability in hormonal control mechanisms, but TSH is generally stimulated by decreasing T4 levels."
16	4	The word "both" here may be confusing with this sentence structure –

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
		consider deleting.
16	8	The HPT axis should be assumed to be intact in all individuals, which this sentence suggests again. Recommend replacing the phrase "involved with regulating thyroid hormone concentrations" with "perturbed".
16	14	Recommend deleting "just"
17	3	Should be "conditions"
17	8	Suggest replacing "Elevated TSH levels" with "Elevated serum TSH concentrations"
17	13-14	Suggest replacing "euthyroid conditions occur for" with "euthyroidism is defined as", and "hypothyroxinemia occurs for" with "hypothyroxinemia is defined as"
17	20-21	Typos in this sentence with the missing end parentheses and double period.
18	19	Note that the recommended iodine intake for lactating women of 250 mcg/day is that by the WHO, UNICEF, and ICCIDD (now IGN), but the U.S. Institute of Medicine has a slightly different recommendation of 290 mcg/day for lactating women.
20	1	Insert: "For the formula-fed infant, the age-specific mean fT4 concentration was defined…"
21	Table 1	• The units of FT4 should be included. • It should be clarified that these are serum FT4 concentrations. It is customary to use the term "full-term" rather than "normal-term" infants.
32	Figure 3	The arrow terminating in "infant ingestion" may be misleading to some and can be better redrawn to clarify that this is not resulting in the set of processes immediately below this (i.e. thyroid plasma refers to the mother, not the infant).
37	6	It can also be cited that the placenta strongly expresses the type III deiodinase (Roti et al; PMID 7263836), thus partially responsible for the high rT3 levels seen at birth.
61	3	Typo: Should be cow milk-based formula
61	6-12	Suggest use of the term "urinary perchlorate concentrations" throughout this paragraph to minimize potential confusion
80	14	The subscript #11 appears to be a typo and can be deleted

Michael H. Lumpkin, Ph.D., DABT

No specific observations on Model Report provided.

Elizabeth N. Pearce, M.D., M.Sc.

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
6	20	"thyroid hormone excretion" would be better worded as "thyroid hormone synthesis and secretion"
16	Footnote 4	"mechanistically it is known that TSH production and release are stimulated by decreasing T4 levels": it is primarily decreased T3 (converted locally from T4 by type 2 deiodinase), that provides feedback at the pituitary and hypothalamus
18	1-3	"The pregnancy model was primarily developed and calibrated using an assumed iodine intake of 200 mcg/d, the level recommended for pregnant women": The Institute of Medicine's RDA for pregnancy is 220 mcg daily. The WHO recommends 250 mcg (WHO Secretariat, Andersson M, de Benoist B, Delange F, Zupan J. Prevention and control of iodine deficiency in pregnant and lactating women and in children less than 2-years-old: conclusions and recommendations of the Technical Consultation. Public Health Nutr. 2007;10(12A):1606-11).
18	19-20	"The lactating mother model was primarily calibrated or tuned assuming iodine ingestion of 250 mcg/d, the level recommended for breast-feeding women.": The Institute of Medicine's RDA for lactation is 290 mcg daily. WHO recommends 250 mcg.
33	12	It is noted that infant plasma volume was calculated based on a study with an n of only 4. Are there more robust data available?
47	Table 6	It is unclear to me why the estimated body weight for lactating women would start out higher (74.6 kg) than that for women in the late third trimester of pregnancy (72.3 kg).
64 and 82		It is noted, per a personal communication from Ben Blount that iodine levels decrease with storage time of breast milk samples. This simply does not make sense if measurement techniques are adequate. There could be some degradation of matrices which might affect iodine measurements by some methods, but the iodine can't actually leave the sample.

Stephen M. Roberts, Ph.D.

Significant observations and comment on the document are provided in the responses to charge questions above.

Joanne F. Rovet, Ph.D.

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
1		Title is not accurate re "pregnant mother and fetus"
6	20-21	This assumption is not clear to me and I don't agree with it
7	13-14	This was confusing to me
7	27	Grammar – "which" describing wrong referent
8	1-3	Where is the evidence for this?
8	4-5	Where is the evidence for this?
8	15-18	What is the relevance of this statement
8	19	Wouldn't data from preterm cohorts suffice here?
11	15	Add "respectively" after "(hypothyroxinemia)"
12	1-2	I think this conclusion is out of context; it was meant infants versus grown men
12	5-7	I disagree – the real reason for suggesting greater sensitivity of infants than older children was the knowledge that the developing brain had a greater need for thyroid hormone at this earlier age
13	7	Why lactating mothers?
13	23	7-90 days is not the *most sensitive* period of thyroid function maturation; clearly gestational thyroid-hormone deficiency also has a major impact, particularly on behavior and vulnerability to later mental health issues
17	15	I am not happy with defining hypothryxinemia for fT4 from 2.5-10th percentiles; Most studies are at least below 5th percentile. This is a statistical decision for studying effects, not a clinical condition
19	21-22	I don't understand this
20	8-11	Too technical
20	16-22	Please cite proper evidence
21	4	Remove "for example" - repeated
42	14	Add "in" before "umen"
43	4-5	Where does this idea come from – not sure it is true
43	5-6	Why? Where?
43	8-9	Why?
43	14	Comma after T3
43	14-15	Why?
44	5-6	Remove brackets around "McLanahan
44	6	"(see also U.S. EPA, 2009)
60	2	Perhaps cite Figure numbers in brackets
60	9	On what basis? Too vague.
60	16-22	Long sentence, hard to read
66	10-13	Confusing
67	11	Vague – what do you mean by "considered adequate"
70	11-13	Also Figure 10: where do these data come from?

Specific Observations on Model Report		
Page	***Line***	***Comment or Question***
77		Figure 14 Right – what is meant by "maternal iodine: 75 µg/d)"? Is this relevant?
78	8	Comma after "100 µg/L"
78	7-10	Long sentence, difficult to follow; not sure how you draw conclusion in sentence – where is the data
79	15	Where do reference values for fT4 come from
80	5-6	Not clear
80	14	"11": Actually, the Vulsma paper predict ~40%
80	11-13	Where are the data in Leung et al 2012? Did she provide the authors with the raw data as they only report correlational results?
83	11	Replace "birth" with "day 7"
84	1-3	Where are these data?

VI. SPECIFIC OBSERVATIONS ON MODEL APPENDICES

Hugh A. Barton, Ph.D.

No specific observations on Model Appendices provided.

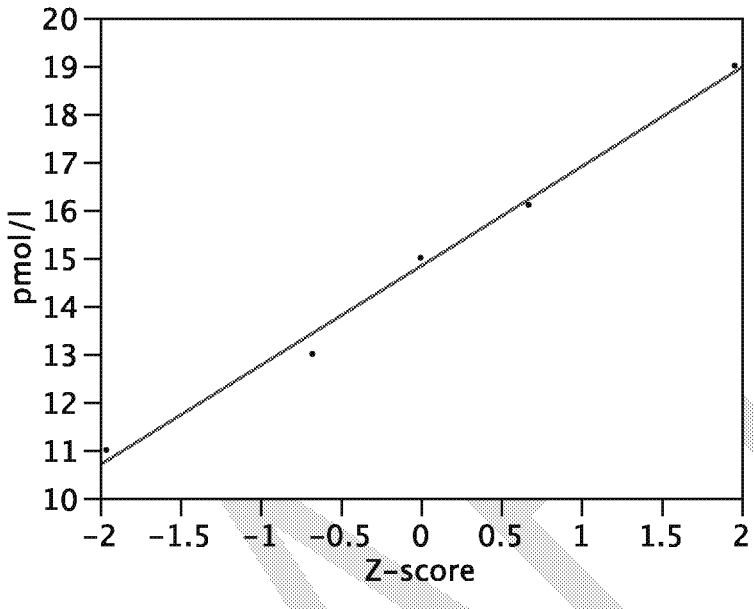
Claude Emond, Ph.D.

No specific observations on Model Appendices provided.

Dale Hattis, Ph.D.

Specific Observations on Model Appendices		
Page	***Line***	***Comment or Question***
App-11	7-10	The fit in figure B-5 is clearly improved over the one that simply went through the lowest point. However the fit should be by inverse-variance weighted least squares not informal choose a value and evaluate fit by eye.
App-12	40-42	Why not assume an actual estimate of either national average or local perchlorate water and food exposures in the area where Greer et al. drew their subjects?
App-24 and -25		There is no specific analysis of the assembled data to evaluate the fit of simpler normal or lognormal distributions to the different observations and justify the use of the more complex lambda sigma model, which has one more parameter than a lognormal. I generated the following for simple normal and lognormal distributions for selected data sets with the most complete descriptions of the information. Overall, lognormal distributions seem to provide adequate fits, and although normal distributions provide a marginally better fit in a few specific cases, there is one case (Wang et al. first trimester) where the normal distribution falls conspicuously short in the fit as measured by the R squared statistic. I doubt that an Akaike information criterion test would find that the extra parameter needed for the lambda sigma distribution model would be justified.

Specific Observations on Model Appendices		
Page	***Line***	***Comment or Question***
App-24 and -25		**Gong and Hoffman (2008) 1st trimester: Normal Distribution Fit**



Linear Fit

pmol/l = 14.82 + 2.068086*Z-score

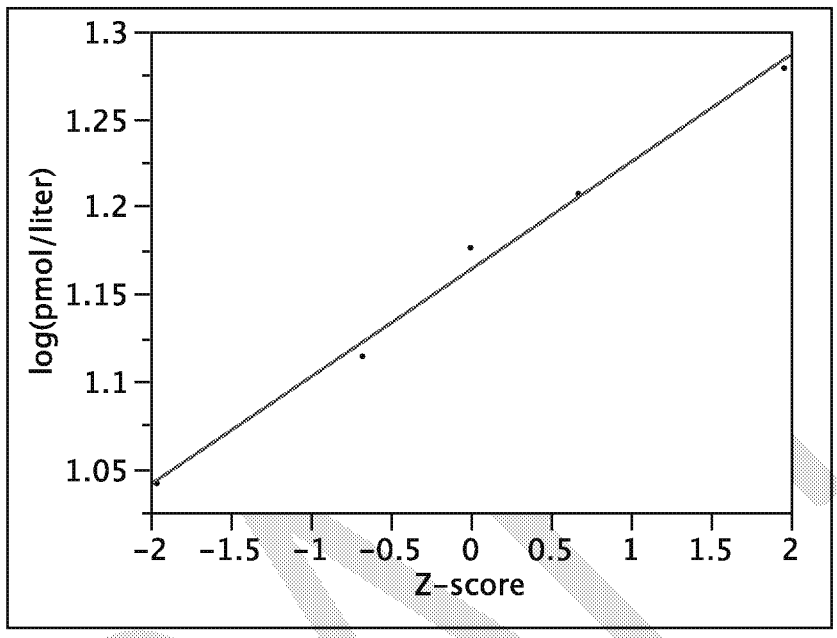
Summary of Fit

RSquare	0.991989
RSquare Adj	0.989318
Root Mean Square Error	0.314541
Mean of Response	14.82
Observations (or Sum Wgts)	5

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	14.82	0.140667	105.36	<.0001
Z-score	2.068086	0.107303	19.27	0.0003

Specific Observations on Model Appendices		
Page	***Line***	***Comment or Question***
		Gong and Hoffman (2008) 1st trimester: **Lognormal Distribution Fit**



Linear Fit
log(pmol/liter) = 1.1634014 + 0.0614314*Z-score

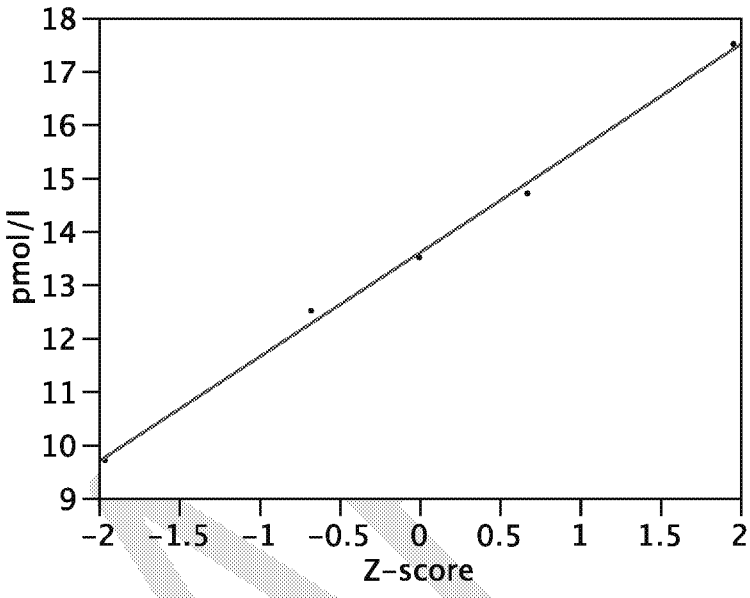
Summary of Fit

RSquare	0.992123
RSquare Adj	0.989498
Root Mean Square Error	0.009264
Mean of Response	1.163401
Observations (or Sum Wgts)	5

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	1.1634014	0.004143	280.82	<.0001
Z-score	0.0614314	0.00316	19.44	0.0003

Specific Observations on Model Appendices		
Page	***Line***	***Comment or Question***
		Gong and Hoffman (2008) 2nd trimester **Normal Distribution Fit**



Linear Fit
pmol/l = 13.58 + 1.9518219*Z-score

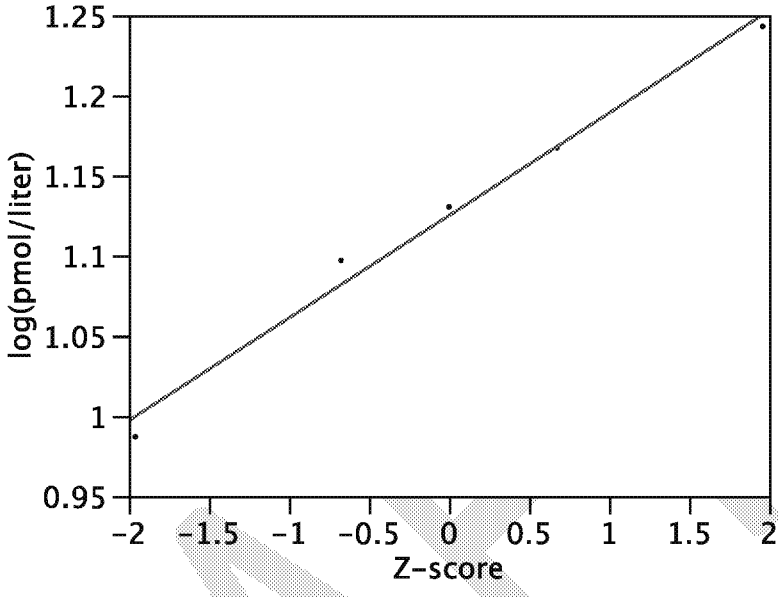
Summary of Fit

RSquare	0.996565
RSquare Adj	0.99542
Root Mean Square Error	0.193934
Mean of Response	13.58
Observations (or Sum Wgts)	5

Parameter Estimates

Term	Estimate	Std Error	t Ratio
Intercept	13.58	0.08673	156.58
Z-score	1.9518219	0.066159	29.5

Specific Observations on Model Appendices		
Page	***Line***	***Comment or Question***
		Gong and Hoffman (2008) 2nd trimester **Lognormal Distribution Fit**



Linear Fit

log(pmol/liter) = 1.1248742 + 0.0639794*Z-score

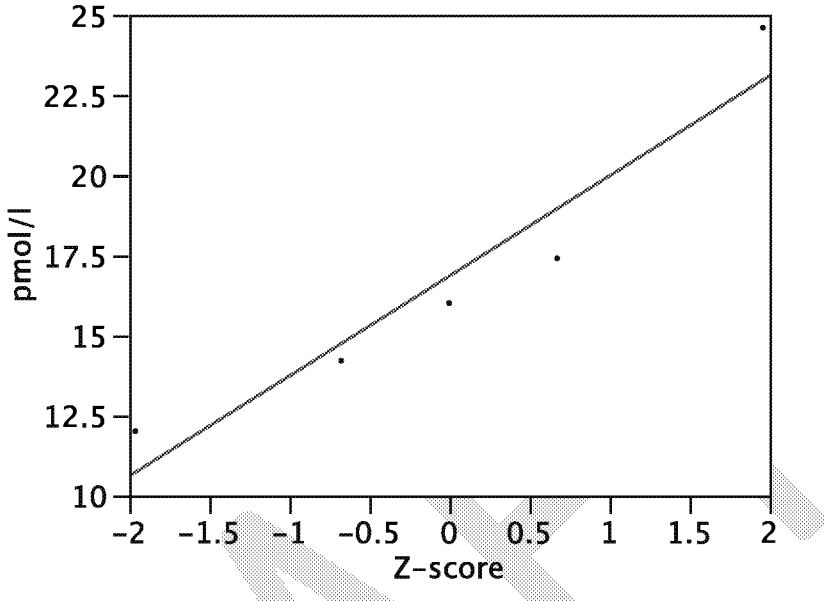
Summary of Fit

RSquare	0.986682
RSquare Adj	0.982242
Root Mean Square Error	0.01258
Mean of Response	1.124874
Observations (or Sum Wgts)	5

Parameter Estimates

Term	Estimate	Std Error	t Ratio
Intercept	1.1248742	0.005626	199.94
Z-score	0.0639794	0.004292	14.91

Specific Observations on Model Appendices		
Page	***Line***	***Comment or Question***
		Wang et al. (2011) 1st trimester (random sample of women) **Normal Distribution Plot**



Linear Fit

pmol/l = 16.84 + 3.1251679*Z-score

Summary of Fit

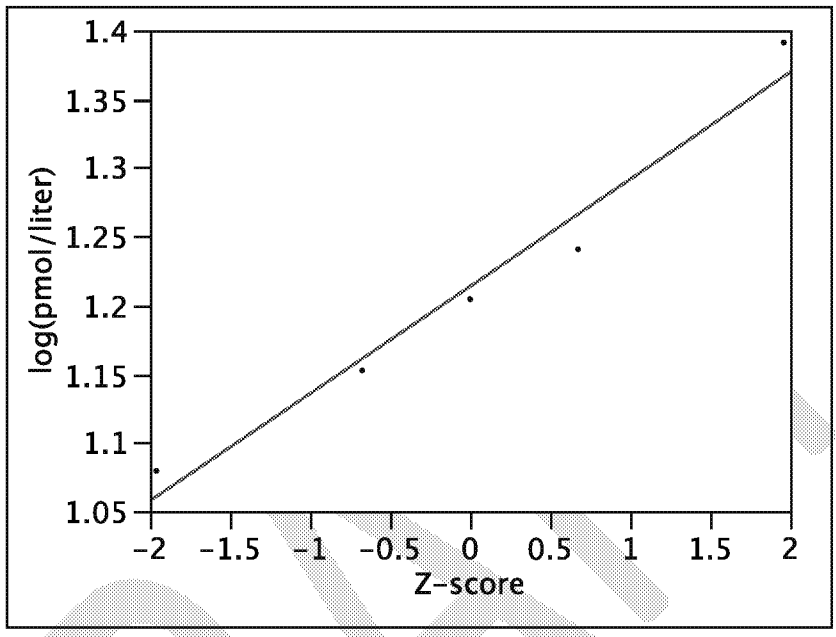
RSquare	0.91587
RSquare Adj	0.887827
Root Mean Square Error	1.603019
Mean of Response	16.84
Observations (or Sum Wgts)	5

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	16.84	0.716892	23.49	0.0002
Z-score	3.1251679	0.546854	5.71	0.0106

Specific Observations on Model Appendices		
Page	***Line***	***Comment or Question***

Wang et al. (2011) 1st trimester (random sample of women)
Lognormal Distribution Plot



Linear Fit
log(pmol/liter) = 1.2134148 + 0.0780372*Z-score

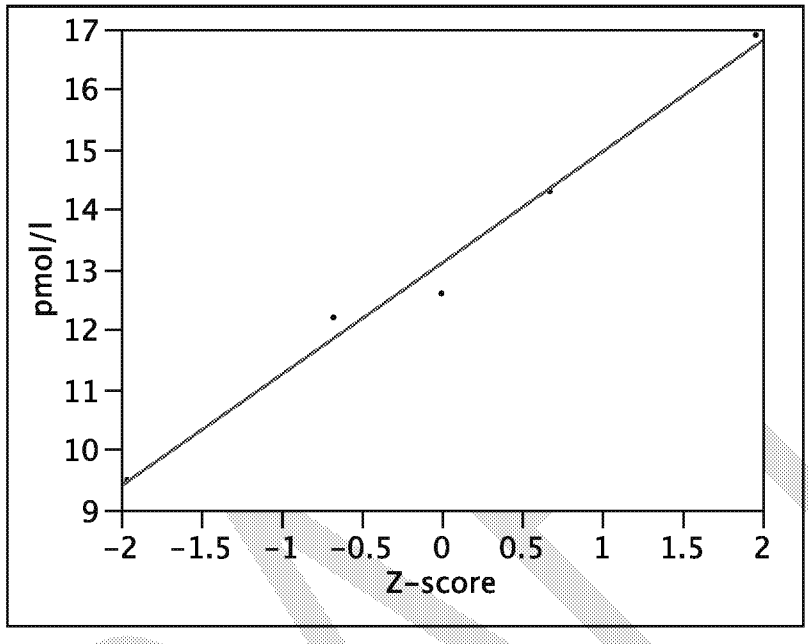
Summary of Fit

RSquare	0.967411
RSquare Adj	0.956548
Root Mean Square Error	0.02424
Mean of Response	1.213415
Observations (or Sum Wgts)	5

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	1.2134148	0.010841	111.93	<.0001
Z-score	0.0780372	0.008269	9.44	0.0025

Specific Observations on Model Appendices		
Page	***Line***	***Comment or Question***
		Wang et al. (2011) 2nd trimester (random sample of women) **Normal Distribution Plot**



Linear Fit
pmol/l = 13.1 + 1.8527348*Z-score

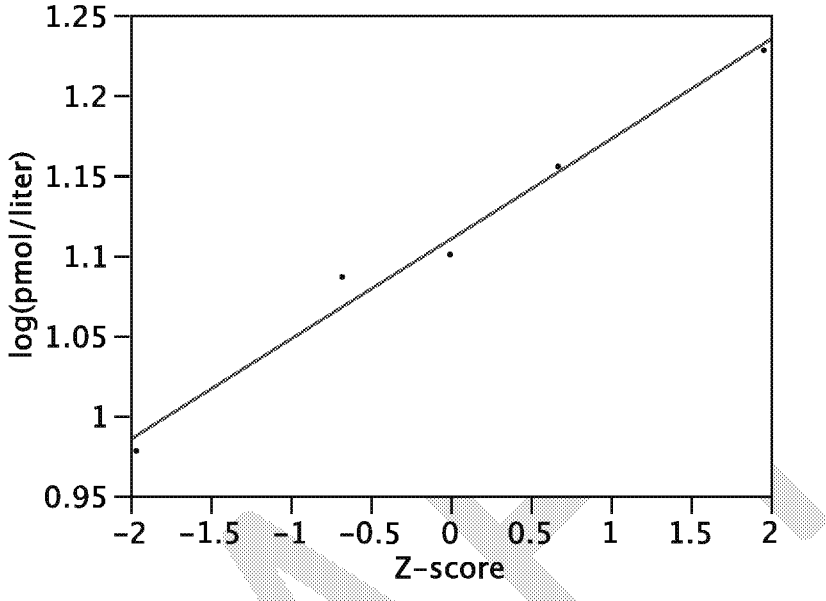
Summary of Fit

RSquare	0.986483
RSquare Adj	0.981977
Root Mean Square Error	0.367043
Mean of Response	13.1
Observations (or Sum Wgts)	5

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	13.1	0.164147	79.81	<.0001
Z-score	1.8527348	0.125213	14.8	0.0007

Specific Observations on Model Appendices		
Page	***Line***	***Comment or Question***
		Wang et al. (2011) 2nd trimester (random sample of women) **Lognormal Distribution Plot**



Linear Fit

log(pmol/liter) = 1.1095353 + 0.062475*Z-score

Summary of Fit

RSquare	0.983535
RSquare Adj	0.978047
Root Mean Square Error	0.01368
Mean of Response	1.109535
Observations (or Sum Wgts)	5

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|
Intercept	1.1095353	0.006118	181.35	<.0001
Z-score	0.062475	0.004667	13.39	0.0009

Angela M. Leung, M.D., M.Sc.

No specific observations on Model Appendices provided.

Michael H. Lumpkin, Ph.D., DABT

No specific observations on Model Appendices provided.

Elizabeth N. Pearce, M.D., M.Sc.

Specific Observations on Model Appendices		
Page	***Line***	***Comment or Question***
App-17	7-10	"Also, the lactating mother has the demands of lactation, which clears iodide and T4 from her system. The mother's basal levels of fT4... are seen to decline 23% from postnatal day 7 to 90, which may be in part because the rate of milk ingestion, hence clearance of iodide and T4, is increasing": lactation does clear significant iodine from the system, but only a very trivial amount of thyroid hormone is secreted into breast milk, certainly not enough to contribute substantially to a decrease in maternal FT4.
App-17	21-22 and 30	It is noted in lines 21-22 that maternal fT4 stabilizes after 2-3 weeks postpartum (which makes sense, given that the half-life of TBG is about 5 days and that of T4 is about 8 days), but this seems to be partially contradicted by the statement in line 30 that maternal serum fT4 decreases with time. Line 30 refers to the right panel of Figure D-4, but I think it should be the right panel of figure C-1.
App-25	Table E-1	As noted above, it would be helpful to provide more information about study cohorts here, particularly with respect to exclusion of TPO and/or thyroglobulin antibody positive women and the population iodine status
App-34	9-10	With respect to pregnant women, "The amount of free iodide in the thyroid was assumed to be a very small quantity, negligible compared to the flux in and out": This is not consistent with the knowledge that the average adult thyroid in iodine-sufficient regions contains 10-20 mg of iodine (accounted for by the CTGIPOOL variables in the infants and lactating mothers).
App-36	18-22	It is noted that in infants if T4 production declines there will be a compensatory increase in the relative rate of T3 production. This is appropriate. However, it is stated that "This mechanism is not assumed to apply in the mother": It is unclear why this is not assumed in the mother, particularly because increases in the maternal ratio of T3:T4 in pregnancy produced could have deleterious effects on the fetus.

Stephen M. Roberts, Ph.D.

No specific observations on Model Appendices provided.

Joanne F. Rovet, Ph.D.

No specific observations on Model Appendices provided.

VII. SPECIFIC OBSERVATIONS ON MODEL CODE

Hugh A. Barton, Ph.D.

No specific observations on Model Code provided.

Claude Emond, Ph.D.

Specific Observations on Model Code: 3352514 - Perchlorate-Iodide-Thyroid-Hormone BBDR Model for the Pregnant Mother and Fetus – acslX version	
File	***Comment or Question***
BBDRHPT_apr2015.csl	Line 26 Why a fix CONSTANT BW_f = 3.4 ! kg| Fetal BW at ~40th Gwk. Is it only the week 40th simulated?
	Line 79 is it the mass balance (MassB_Amount_i). Should not it be at 0?
BBDRPregModel2013.m	This file does not work. Error message

Specific Observations on Model Code: 3352515 - Perchlorate-Iodide-Thyroid-Hormone BBDR Model for the Lactating Mother and Infant – acslX version	
File	***Comment or Question***
ClO4 Fisher infant 2015	Line 428, 432, 435; why do you use variable clearance table function with time
	Line 518 and 526; the constant value are they refereed to Schlosser (2016)? If so add the reference.

Dale Hattis, Ph.D.

No specific observations on Model Code provided.

Angela M. Leung, M.D., M.Sc.

No specific observations on Model Code provided.

Michael H. Lumpkin, Ph.D., DABT

No specific observations on Model Code provided.

Elizabeth N. Pearce, M.D., M.Sc.

No specific observations on Model Code provided.

Stephen M. Roberts, Ph.D.

No specific observations on Model Code provided.

Joanne F. Rovet, Ph.D.

No specific observations on Model Code provided.

Message

From: Perkinson, Russ [Perkinson.Russ@epa.gov]
Sent: 1/5/2017 11:50:16 AM
To: Olson, Daniel [Olson.Daniel@epa.gov]
CC: Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Pre-Meeting comments
Attachments: Pre-Meeting Comment Report for Perchlorate.docx; List of Registered Observers for Perchlorate.pdf

Dan – FYI, here's the pre-meeting comments from peer reviewers. I haven't looked over them and probably won't in any detail, so hoping you can.
Thanks,
Russ

From: Riley, Karie [mailto:KRiley@versar.com]
Sent: Wednesday, January 04, 2017 5:45 PM
To: Perkinson, Russ <Perkinson.Russ@epa.gov>
Subject: Pre-Meeting comments

Hi Russ,

Please find attached the pre-meeting comments and list of observers. We have sent these and the agenda to the reviewers.

Karie

Karie Riley
Environmental Services Group
Versar, Inc.
6850 Versar Center
Springfield, VA 22151
Direct Line: (703) 642-6915
Fax: (703) 642-6809
Email: kriley@versar.com
Visit us at: www.versar.com

Message

From: Olson, Daniel [Olson.Daniel@epa.gov]
Sent: 2/15/2017 7:39:13 PM
To: Benson, Bob [Benson.Bob@epa.gov]; Cantilli, Robert [Cantilli.Robert@epa.gov]; Chiu, Enid [Chiu.Enid@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Crofton, Kevin [Crofton.Kevin@epa.gov]; Dockins, Chris [Dockins.Chris@epa.gov]; El-Burai-Felix, Alia [el-burai-felix.alia@epa.gov]; Firestone, Michael [Firestone.Michael@epa.gov]; Flaharty, Stephanie [Flaharty.Stephanie@epa.gov]; Flowers, Lynn [Flowers.Lynn@epa.gov]; Foos, Brenda [Foos.Brenda@epa.gov]; Georges, Jessica [Georges.Jessica@epa.gov]; Gilbert, Mary E. [Gilbert.Mary@epa.gov]; Hafez, Ahmed [Hafez.Ahmed@epa.gov]; Harmon, Kenneth [Harmon.Kenneth@epa.gov]; Helm, Erik [Helm.Erik@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Johnson, Ann [Johnson.Ann@epa.gov]; Jones, Joel E. [Jones.Joel@epa.gov]; Kapraun, Dustin [Kapraun.Dustin@epa.gov]; Kirk, Andrea [Kirk.Andrea@epa.gov]; Li, Corine [Li.Corine@epa.gov]; Macler, Bruce [Macler.Bruce@epa.gov]; Messier, Dawn [Messier.Dawn@epa.gov]; Miller, Gregory [Miller.Gregory@epa.gov]; Morrison, Kendra [Morrison.Kendra@epa.gov]; Schlosser, Paul [Schlosser.Paul@epa.gov]; Perkinson, Russ [Perkinson.Russ@epa.gov]; Raffaele, Kathleen [raffaele.kathleen@epa.gov]; Schutz, Michelle [Schutz.Michelle@epa.gov]; Cooperstein, Sharon [Cooperstein.Sharon@epa.gov]; Skaar, Christina [Skaar.Christina@epa.gov]; Strong, Jamie [Strong.Jamie@epa.gov]; Townsend, Clifton [Townsend.Clifton@epa.gov]; El-Burai-Felix, Alia [el-burai-felix.alia@epa.gov]
CC: kinetics@leavens.us
Subject: Perchlorate Update & Draft Peer Review Report
Attachments: Perchlorate Peer Review Report_TO 2015-22_Draft.docx; Feb 15 Perchlorate Update FINAL.ps.docx

Perchlorate Workgroup Members,

Please find attached for your information an update on the expansion perchlorate BBDR model and MCLG approach report to early pregnancy and the Draft External Peer Review Report of the BBDR Model and Report.

Thanks,

Dan

From: Olson, Daniel
Sent: Wednesday, February 08, 2017 12:11 PM
To: Benson, Bob <Benson.Bob@epa.gov>; Cantilli, Robert <Cantilli.Robert@epa.gov>; Chiu, Enid <Chiu.Enid@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Crofton, Kevin <Crofton.Kevin@epa.gov>; Dockins, Chris <Dockins.Chris@epa.gov>; El-Burai-Felix, Alia <el-burai-felix.alia@epa.gov>; Firestone, Michael <Firestone.Michael@epa.gov>; Flaharty, Stephanie <Flaharty.Stephanie@epa.gov>; Flowers, Lynn <Flowers.Lynn@epa.gov>; Foos, Brenda <Foos.Brenda@epa.gov>; Georges, Jessica <Georges.Jessica@epa.gov>; Gilbert, Mary E. <Gilbert.Mary@epa.gov>; Hafez, Ahmed <Hafez.Ahmed@epa.gov>; Harmon, Kenneth <Harmon.Kenneth@epa.gov>; Helm, Erik <Helm.Erik@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Johnson, Ann <Johnson.Ann@epa.gov>; Jones, Joel E. <Jones.Joel@epa.gov>; Kapraun, Dustin <Kapraun.Dustin@epa.gov>; Kirk, Andrea <Kirk.Andrea@epa.gov>; Li, Corine <Li.Corine@epa.gov>; Macler, Bruce <Macler.Bruce@epa.gov>; Messier, Dawn <Messier.Dawn@epa.gov>; Miller, Gregory <Miller.Gregory@epa.gov>; Morrison, Kendra <Morrison.Kendra@epa.gov>; Olson, Daniel <Olson.Daniel@epa.gov>; 'Paul Schlosser' <schlosser.paul@epa.gov>; Perkinson, Russ <Perkinson.Russ@epa.gov>; Raffaele, Kathleen <raffaele.kathleen@epa.gov>; Schutz, Michelle <Schutz.Michelle@epa.gov>; 'Sharon Cooperstein' <cooperstein.sharon@epa.gov>; Skaar, Christina <Skaar.Christina@epa.gov>; Strong, Jamie <Strong.Jamie@epa.gov>; Townsend, Clifton <Townsend.Clifton@epa.gov>
Cc: kinetics@leavens.us
Subject: Update on Perchlorate BBDR Model Revisions and MCLG Approach

Perchlorate Workgroup Members,

As we discussed at our last workgroup meeting, please find attached for your information an update on revisions to the perchlorate BBDR model and MCLG approach. The revisions are based on panel member recommendations discussed at the peer review meeting (we have not received the draft panel report).

Thanks,

Dan

Expansion of BBDR model and MCLG Approach to Early Pregnancy
February 15, 2017 Update

Draft Peer Review Report

- Versar recently provided EPA with the Draft Peer Review Report for review
- BBDR model team is reviewing, initial/cursory review -
    - Report confirms the direction of the work underway to model early pregnancy and conduct additional uncertainty analysis
    - Report also states that, "a model is never done" and recommends that at some point EPA use the model as-is and make additional refinements in the future. Examples provided include co-exposure to other goitrogens, compensatory effects in response to perchlorate inhibition and probabilistic inputs.
    - If necessary, EPA reviewers may send 2-3 clarifying questions back to Versar before finalizing the report.
- Moving forward, the BBDR model team has agreed to:
    - Continue modeling early pregnancy
    - Qualitatively discuss other goitrogens rather than quantitatively featuring them as part of the BBDR model
    - Continue investigating how to address TSH feedback with regard to Human Chorionic Gonadotropin (hCG) feedback *in utero*
    - Seek input from ORD thyroid experts

Model extrapolation to early pregnancy – *continuation of work*

- Dr. Schlosser (EPA/ORD/NCEA) is editing primary model code
- Dr. Leavens (ORNL contractor) working on growth equations
- Initial early pregnancy data obtained from contractor
- Next steps: Abt to provide T4, fT4, T3 data for non-pregnant woman (childbearing age) as a function of time in/through first trimester

Uncertainty analysis

- Dr. Kapraun (EPA/ORD/NCEA) has version of model code and statistical model for Bayesian analysis prepared, successful test with simulated data
- Next steps: Dr. Gay Goodman has transmitted Greer study data to EPA (both radio-iodide uptake and perchlorate blood and urinary data expected). Further discussions are warranted.

Continued evaluation of other goitrogens and data on fT4-TSH relationship in NHANES data (2011-2012)

MCLG approach

- The Approach report is being updated to include the additional studies found in the updated literature search.
- The Korevaar data is being analyzed. Clarification questions on the organization of the data sets have been asked of Korevaar in order to reproduce his analysis and then derive a continuous dose response function.
- An outline of a revised MCLG Approach report to accommodate an expanded BBDR model has been drafted and reviewed by Abt.
- Additional thyroid hormone data has been compiled per Dr. Schlosser's request. A teleconference with Dr. Schlosser will take place this week to transfer the information and identify additional data.

Message

From: Huff, Lisa [Huff.Lisa@epa.gov]
Sent: 6/29/2017 12:38:24 PM
To: Albert, Ryan [Albert.Ryan@epa.gov]
CC: Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]
Subject: FW: Quick Turnaround.....Fwd: FOR YOUR REVIEW: FFRRO Technical Fact Sheets Update
Attachments: 1-4-Dioxane fact sheet update 5-26-17_508.pdf; ATT00001.htm; FFRRO Fact Sheet -DNT_2-7-17_508.pdf; ATT00002.htm; FFRRO Fact Sheet-Nanomaterials_4-28-17.pdf; ATT00003.htm; FFRRO FactSheet PBDE-PBB update 1-23-17_508.pdf; ATT00004.htm; FFRRO_ECFactSheet_RDX_4-24-17_508.pdf; ATT00005.htm; FFRRO_ECFactSheet_Tungsten_ 4-24-17.pdf; ATT00006.htm; FFRROFactSheet_Contaminants_PFOS PFOA_4-11-17.pdf; ATT00007.htm; FFRROFactSheet_Contaminants_TCP_1-23-17_508.pdf; ATT00008.htm; FFRROFactSheet_Contaminants_TNT_1-23-16_508.pdf; ATT00009.htm; NDMA fact sheet update 1-19-17_508.pdf; ATT00010.htm; Perchlorate_FactSheet 4-24-17.pdf; ATT00011.htm

Ryan,
We can discuss how we want to divide these up between CCL and RD folks if that works for you? And we can include TSC for UCMR ones too.

Lisa Foersom Huff

Associate Branch Chief
Targeting and Analysis Branch
Standards and Risk Management Division
Office of Groundwater and Drinking Water
U.S. EPA
EPA East Bldg. Rm. 2357 H
202-566-0787

From: Rodgers-Jenkins, Crystal
Sent: Wednesday, June 28, 2017 5:38 PM
To: Huff, Lisa <Huff.Lisa@epa.gov>; Albert, Ryan <Albert.Ryan@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Carroll, Gregory <Carroll.Gregory@epa.gov>; Hautman, Dan <Hautman.Dan@epa.gov>
Cc: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: Quick Turnaround.....Fwd: FOR YOUR REVIEW: FFRRO Technical Fact Sheets Update

Deadline - due to Ann by COB tomorrow

Would you please have your staff do a quick review of the fact sheets for our priority contaminants (e.g., contaminants on CCL, reg det lists)? Please note the fact sheets for PFOA, PFOS, perchlorate are on hold.

I am reading the request from my iphone so I haven't opened all the files...1,4-dioxane, ndma, Rdx are a few of the ones i've opened thus far.

Sent from my iPhone

Begin forwarded message:

> **From:** "Tricas, Marisa" <tricas.marisa@epa.gov>
> **To:** "Mclain, Jennifer" <Mclain.Jennifer@epa.gov>, "Burneson, Eric" <Burneson.Eric@epa.gov>, "Rodgers-Jenkins, Crystal" <Rodgers-Jenkins.Crystal@epa.gov>
> **Cc:** "Grevatt, Peter" <Grevatt.Peter@epa.gov>, "Carroll, Gregory" <Carroll.Gregory@epa.gov>,

"Wadlington, Christina" <Wadlington.Christina@epa.gov>
Subject: FW: FOR YOUR REVIEW: FFRRO Technical Fact Sheets Update

All,

OLEM has provided technical factsheets for final round of review to seek OPA approval to post on the web. PFOA, PFOS and Perchlorate factsheets are on hold.

Lee has asked a quick turnaround – Ann wants an update on where we are COB tomorrow.

Sincerely,

Marisa Tricas
Communications Specialist (on detail to the Immediate Office)
Office of Ground Water and Drinking Water
Office of Water
United States Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington, D.C. 20004
Phone: 202-564-2955
Office: WJC East 2104D
Website: https://www.epa.gov/ground-water-and-drinking-water

From: Campbell, Ann
Sent: Wednesday, June 28, 2017 4:04 PM
To: Grevatt, Peter <Grevatt.Peter@epa.gov>; Southerland, Elizabeth <Southerland.Elizabeth@epa.gov>
Cc: Behl, Betsy <Behl.Betsy@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Christensen, Christina <Christensen.Christina@epa.gov>; Tricas, Marisa <tricas.marisa@epa.gov>
Subject: FOR YOUR REVIEW: FFRRO Technical Fact Sheets Update

Folks, I'm hoping this is an easy lift. OLEM has provided the attached technical fact sheets for one last round of review prior to seeking OPA approval to post. My sense is to the extent they impact us, you all have been engaged already. Please let me know if you have any comments on the attached. Note that the PFOA?PFOS and Perchlorate factsheets have been put on hold so they are not part of this package.

Lee has asked for our review with all deliberate speed. If you could give me a sense of where you're at in your review by COB tomorrow, I'd greatly appreciate it.

If you have any questions, please let me know!
Ann

From: Forsgren, Lee
Sent: Wednesday, June 28, 2017 3:54 PM
To: Campbell, Ann <Campbell.Ann@epa.gov>
Subject: FW: FFRRO Technical Fact Sheets Update

Here is the background materials.

From: Davis, Patrick
Sent: Wednesday, June 28, 2017 3:05 PM

To: Beck, Nancy <Beck.Nancy@epa.gov>; Forsgren, Lee <Forsgren.Lee@epa.gov>; Gunasekara, Mandy <Gunasekara.Mandy@epa.gov>; Bolen, Brittany <bolen.brittany@epa.gov>
Subject: FW: FFRRO Technical Fact Sheets Update

Sending agai with attachments

Patrick Davis
Environmental Protection Agency
Deputy Assistant Administrator, Office of Land and Emergency Management
202-564-3103 office
Ex. 6 Personal Privacy (PP) cell

From: Davis, Patrick
Sent: Monday, June 26, 2017 4:20 PM
To: Beck, Nancy <beck.nancy@epa.gov>; Forsgren, Lee <Forsgren.Lee@epa.gov>; Patrick Traylor (traylor.patrick@epa.gov) <traylor.patrick@epa.gov>; Gunasekara, Mandy <Gunasekara.Mandy@epa.gov>; Bolen, Brittany <bolen.brittany@epa.gov>
Subject: FW: FFRRO Technical Fact Sheets Update

Nancy, Lee, Patrick, Mandy and Brittany,

Attached are Technical fact sheet updates for our review before they are posted to our website. We have put a hold on the PFOA/PFOS and Perchlorate fact sheets. If you see others that raise a red flag please let me know.

Thanks,

Patrick Davis
Environmental Protection Agency
Deputy Assistant Administrator, Office of Land and Emergency Management
202-564-3103 office
Ex. 6 Personal Privacy (PP) cell

From: Cooke, Maryt
Sent: Thursday, June 15, 2017 11:46 AM
To: Breen, Barry <Breen.Barry@epa.gov>; Davis, Patrick <davis.patrick@epa.gov>; Simon, Nigel <Simon.Nigel@epa.gov>; Bertrand, Charlotte <Bertrand.Charlotte@epa.gov>
Cc: Lowery, Brigid <Lowery.Brigid@epa.gov>; Colip, Matthew <colip.matthew@epa.gov>; Young, Dianna <Young.Dianna@epa.gov>; Gervais, Gregory <Gervais.Gregory@epa.gov>
Subject: FFRRO Technical Fact Sheets Update

Barry/Patrick/Nigel –

Ex. 5 Deliberative Process (DP)

Ex. 5 Deliberative Process (DP)

We sent these to CPA in anticipation of getting your approval to move forward. Once approve they will continue through the OPA process.

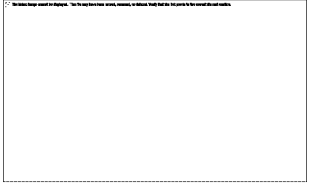
Please let me know if you have any questions or require any additional information. I look forward to your feedback.

Thank you

Mary T. Cooke
USEPA Headquarters
William Jefferson Clinton Building
1200 Pennsylvania Avenue, N. W.
Mail Code: 5106R (FFRRO)
Washington, DC 20460

Phone: 202-564-0788

Learn about Federal Facility Cleanups in your area:



Message

From: Hafez, Ahmed [Hafez.Ahmed@epa.gov]
Sent: 2/1/2017 7:38:00 PM
To: Olson, Daniel [Olson.Daniel@epa.gov]; Beasley, Lynn [Beasley.Lynn@epa.gov]; Benson, Bob [Benson.Bob@epa.gov]; Cantilli, Robert [Cantilli.Robert@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Cooperstein, Sharon [Cooperstein.Sharon@epa.gov]; Crofton, Kevin [Crofton.Kevin@epa.gov]; Dockins, Chris [Dockins.Chris@epa.gov]; Firestone, Michael [Firestone.Michael@epa.gov]; Flaharty, Stephanie [Flaharty.Stephanie@epa.gov]; Flowers, Lynn [Flowers.Lynn@epa.gov]; Foos, Brenda [Foos.Brenda@epa.gov]; Gilbert, Mary E. [Gilbert.Mary@epa.gov]; Harmon, Kenneth [Harmon.Kenneth@epa.gov]; Helm, Erik [Helm.Erik@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Jones, Joel E. [Jones.Joel@epa.gov]; Li, Corine [Li.Corine@epa.gov]; Macler, Bruce [Macler.Bruce@epa.gov]; Perkinson, Russ [Perkinson.Russ@epa.gov]; Schlosser, Paul [Schlosser.Paul@epa.gov]; Schutz, Michelle [Schutz.Michelle@epa.gov]; Skaar, Christina [Skaar.Christina@epa.gov]; Townsend, Clifton [Townsend.Clifton@epa.gov]; Raffaele, Kathleen [raffaele.kathleen@epa.gov]; Johnson, Ann [Johnson.Ann@epa.gov]; Chiu, Enid [Chiu.Enid@epa.gov]; Nahar, Muna [Nahar.Muna@epa.gov]; Strong, Jamie [Strong.Jamie@epa.gov]; Messier, Dawn [Messier.Dawn@epa.gov]; Kirk, Andrea [Kirk.Andrea@epa.gov]; Georges, Jessica [Georges.Jessica@epa.gov]; Morrison, Kendra [Morrison.Kendra@epa.gov]; Kapraun, Dustin [Kapraun.Dustin@epa.gov]; Miller, Gregory [Miller.Gregory@epa.gov]
CC: Noyes, Pamela [Noyes.Pamela@epa.gov]; Clifton Townsend Ex. 6 Personal Privacy (PP)
Subject: RE: Perchlorate Workgroup Meeting
Attachments: Korevaar et al. - 2016 - Association of maternal thyroid function during ea.pdf

Hello all,

Attached is the Korevaar study mentioned in the Work Group Meeting held on February 1st.

Regards,

Ahmed

Korevaar et al. - 2016 - Associatio...

Ahmed M. Hafez, Ph.D.
OW/OGWDW/SRMD/TAB | Office: WJC East 2227Q
hafez.ahmed@epa.gov | phone: 202.564.1944

"It is better to do things that you cannot explain, than to explain things that you cannot do."
--Nassim Taleb

-----Original Appointment-----
From: Olson, Daniel
Sent: Wednesday, April 27, 2016 7:54 AM
To: Olson, Daniel; Beasley, Lynn; Benson, Bob; Cantilli, Robert; Christ, Lisa; Cooperstein, Sharon; Crofton, Kevin; Dockins, Chris; Firestone, Michael; Flaharty, Stephanie; Flowers, Lynn; Foos, Brenda; Gilbert, Mary E.; Gray, Fredianne; Harmon, Kenneth; Helm, Erik; Hernandez-Quinones, Samuel; Jones, Joel E.; Li, Corine; Macler, Bruce; Perkinson, Russ; Schlosser, Paul; Schutz, Michelle; Skaar, Christina; Townsend, Clifton; Raffaele, Kathleen; Johnson, Ann; Chiu, Enid; Nahar, Muna; Strong, Jamie; Messier, Dawn; Kirk, Andrea; Georges, Jessica; Hafez, Ahmed; Morrison, Kendra; Kapraun, Dustin; Miller,

Gregory
Cc: Noyes, Pamela; Fultz, Christopher; Clifton Townsend
Subject: Perchlorate Workgroup Meeting
When: Wednesday, February 01, 2017 2:00 PM-3:00 PM (UTC-05:00) Eastern Time (US & Canada).
Where: Conference Room 2123 East

The purpose of the meeting is to report out on the January 10 and 11 peer review meeting and next steps - revision of the BBDR model and report, revision of the MCLG approach report and second panel.

Change in conference room to 2123 east.

Dial in number is Ex. 6 Personal Privacy (PP)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

January 18, 2017

Tom Neltner and Maricel Maffini
Natural Resources Defense Council
1152 15th Street NW, Suite 300
Washington, D.C. 20005

Re: NRDC-Observations on Tolerances for Hypochlorite to Minimize Degeneration to Perchlorate, Correspondence Dated July 31, 2014

Dear Mr. Neltner and Ms. Maffini:

Thank you for your July 31, 2014 correspondence presenting NRDC's "observations on tolerances for hypochlorite to minimize degeneration to perchlorate." The letter requests that, during the registration review for sodium and calcium hypochlorite (Na and Ca hypochlorite), the Environmental Protection Agency (EPA) consider setting tolerances for sodium and calcium hypochlorite to limit perchlorate residues. In addition, NRDC suggests that EPA should use the Na and Ca hypochlorite registration review to determine, pursuant to 21 USC § 346a(a)(3), that perchlorate is a degradation product of hypochlorite and is "likely to pose a potential health risk from dietary exposure in food and water that is of a different type than and of a greater significance than the risk posed by dietary exposure to hypochlorite." NRDC recommends that the agency, in assessing the risk of hypochlorite use in food processing, take into consideration the combined effect of perchlorate, thiocyanate, and nitrate on fetuses and infants and aggregate exposure to perchlorate from all sources including hypochlorite and plastic packaging. The letter additionally suggests that hypochlorite pesticide products should have an expiration date to further minimize perchlorate levels. While the letter falls outside of any currently open registration review comment period for Na and Ca hypochlorite, we will post your comments to the docket[1] along with this response.

EPA agrees with the observation in your letter that research by the American Water Works Association and the Water Research Foundation suggest the potential for perchlorate to form in stored hypochlorite solutions.[2] As noted in the research, the American Water Works Association

[1] Registration review of Na and Ca hypochlorite; Docket ID # EPA-HQ-OPP-2012-0004 at www.regulations.gov
[2] Stanford, B.D., A. Pisarenko, S. Snyder, and G. Gordon, Perchlorate, Bromate, and Chlorate in Hypochlorite Solutions: Guidelines for Utilities. Journal - American Water Works Association, 2011. 103(6): p. 71-83. Available at http://www.awwa.org/publications/journal-awwa/abstract/articleid/28067.aspx. And: Stanford, B.D., A.N. Pisarenko, S.A. Snyder, and G. Gordon, Minimizing Perchlorate Formation in Hypochlorite Solutions, Opflow, 2009. 35(10): p. 10-13. http://www.waterrf.org/ExecutiveSummaryLibrary/4147_NON_profile.pdf.

and the Water Research Foundation found hypochlorite concentration, pH, ionic strength, and temperature were major factors impacting perchlorate formation in stored hypochlorite solutions at drinking water utilities.[3] Additionally, recent monitoring data included in the EPA Office of Water's Unregulated Contaminant Monitoring Rule (UCMR 3) found increased levels of chlorate in finished drinking water.[4] Therefore, the agency intends, as part of its next steps in the registration review of Na and Ca hypochlorite, to take an in-depth look at the requests in your letter, including whether any action is appropriate under the FFDCA, and to consider, among other things, possible labeling language to optimize storage of hypochlorite products in order to minimize perchlorate and chlorate formation during storage.

As you know, the EPA Office of Water has begun the National Primary Drinking Water Regulation (NPDWR) process for perchlorate. To inform this effort, EPA and Food and Drug Administration scientists developed a Biologically Based Dose Response (also known as a Physiologically-Based Pharmacokinetic (PBPK)) model to inform the agency's SDWA decision making. In light of this, the Office of Pesticide Programs (OPP) will continue to work with the Office of Water on perchlorate issues during registration review for Na and Ca hypochlorite.

Thank you for your interest and input into the registration review of Na and Ca hypochlorite. We continue to welcome any information that you have or become aware of in the future that relates to this issue and the Na and Ca hypochlorite registration review. If you have any questions concerning this response, please contact Rose Kyprianou at (703) 305-5354 or Kyprianou.Rose@epa.gov.

Sincerely,

Steve Knizner
Director
Antimicrobials Division
Office of Pesticide Programs
U.S. Environmental Protection Agency

[3] Id.
[4] USEPA, Six-Year Review 3 Technical Support Document for Chlorate, December 2016, EPA-810-R-16-013. Available at https://www.epa.gov/sites/production/files/2016-12/documents/810r16013.pdf.

Message

From: Olson, Daniel [Olson.Daniel@epa.gov]
Sent: 11/30/2016 1:22:02 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
CC: Perkinson, Russ [Perkinson.Russ@epa.gov]; Townsend, Clifton [Townsend.Clifton@epa.gov]; Helm, Erik [Helm.Erik@epa.gov]; Carroll, Gregory [Carroll.Gregory@epa.gov]
Subject: FW: Letter to Administrator McCarthy re: Perchlorate Rulemaking
Attachments: psg - bbdr policy letter to admin mccarthy 11.29.16.pdf; ATT00001.htm

Lisa,

In the attached letter the PSG raises a number of concerns including the CD. Their recommendations follow:

- The peer review panel **should** draft the report not Versar;
- Comments **should** be provided to the panel, not a summary;
- Panel recommendations **should** be a consensus not individual perspectives; and
- EPA **should** update occurrence information prior to drafting the HRRCA because:
  - 30% of the UCMR 1 samples were collected at entry points,
  - There has been significant declines in perchlorate occurrence since 2001-2003 (e.g., CA), and
  - UCMR-1 method 314 is prone to false detections and interferences

An initial thought - PSG's recommendations on occurrence are premature as we have yet the review the model, let alone, the vet or review the MCLG approach. Also, I believe that our updated draft Occurrence Report addresses these issues which will be subject to public notice and comment at a later date as part of the perchlorate regulatory action.

I can draft a response highlighting responses to their peer review recommendations then send it to Russ for review unless you would like us to take a different direction.

Thanks,

Dan

From: Burneson, Eric
Sent: Tuesday, November 29, 2016 6:04 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Olson, Daniel <Olson.Daniel@epa.gov>; Carroll, Gregory <Carroll.Gregory@epa.gov>
Subject: Fwd: Letter to Administrator McCarthy re: Perchlorate Rulemaking

Lisa:
We will likely be asked to prepare a response to the attached letter. I am copying Greg because they are raising old UCMR issues.

Sent from my iPhone

Begin forwarded message:

> **From:** "Grevatt, Peter" <Grevatt.Peter@epa.gov>
> **Date:** November 29, 2016 at 4:58:54 PM CST
> **To:** "Burneson, Eric" <Burneson.Eric@epa.gov>
> **Cc:** "Mclain, Jennifer" <Mclain.Jennifer@epa.gov>, "Greene, Ashley" <Greene.Ashley@epa.gov>
> **Subject: FW: Letter to Administrator McCarthy re: Perchlorate Rulemaking**
>
> FYI. I assume this will get controlled to us.

From: Tom Roberts [mailto:tcr@vnf.com]
Sent: Tuesday, November 29, 2016 3:31 PM
To: Mccarthy, Gina <McCarthy.Gina@epa.gov>
Cc: Azoolin, Liel <Azoolin.Liel@epa.gov>; Meiburg, Stan <Meiburg.Stan@epa.gov>; Beauvais, Joel <Beauvais.Joel@epa.gov>; Grevatt, Peter <Grevatt.Peter@epa.gov>; Shapiro, Mike <Shapiro.Mike@epa.gov>
Subject: Letter to Administrator McCarthy re: Perchlorate Rulemaking

Administrator McCarthy – attached please find a letter from the Perchlorate Study Group regarding the peer review process for the biologically-based dose response model for the perchlorate rulemaking under the Safe Drinking Water Act.

Thank you.

Tom Roberts | Partner

Van Ness Feldman LLP

1050 Thomas Jefferson Street, NW
Washington, DC 20007
(202) 298-1930 (o) | (202) 365-7750 (c) | tcr@vnf.com | vnf.com

Message

From: Burneson, Eric [Burneson.Eric@epa.gov]
Sent: 11/28/2016 1:40:00 PM
To: Christ, Lisa [Christ.Lisa@epa.gov]
CC: Olson, Daniel [Olson.Daniel@epa.gov]
Subject: FW: AWWA Comments on BBDR Perchlorate Model
Attachments: AWWA Comments on BBDR Perchlorate Model.pdf

From: Kevin Morley [mailto:KMorley@awwa.org]
Sent: Friday, November 25, 2016 1:20 PM
To: Beauvais, Joel <Beauvais.Joel@epa.gov>
Cc: Grevatt, Peter <Grevatt.Peter@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Perkinson, Russ <Perkinson.Russ@epa.gov>; Southerland, Elizabeth <Southerland.Elizabeth@epa.gov>; Behl, Betsy <Behl.Betsy@epa.gov>; Tracy Mehan <tmehan@awwa.org>
Subject: AWWA Comments on BBDR Perchlorate Model

On behalf of the American Water Works Association, please accept the attached comments regarding the draft Biologically Based Dose-Response (BBDR) model for perchlorate (81 FR 67350; EPA-HQ-OW-2016-0438).

Thank you.

Kevin M. Morley, PhD
American Water Works Association
Manager, Federal Relations
1300 Eye Street, NW Suite 701W
Washington, DC 20005
D: 202-326-6124

Message

From: Perkinson, Russ [Perkinson.Russ@epa.gov]
Sent: 10/25/2016 1:41:06 PM
To: Mudipalli, Anuradha [Mudipalli.Anu@epa.gov]; Perkinson, Russ [Perkinson.Russ@epa.gov]; Grifo, Francesca [Grifo.Francesca@epa.gov]; Greene, Mary [greene.mary@epa.gov]; Rechenberg, Kathleen [Rechenberg.Kathleen@epa.gov]; Anand Mudambi [Mudambi.Anand@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Strong, Jamie [Strong.Jamie@epa.gov]; Ohanian, Edward [Ohanian.Edward@epa.gov]; Olson, Daniel [Olson.Daniel@epa.gov]; Oshida, Phil [Oshida.Phil@epa.gov]; Berger, Philip [Berger.Philip@epa.gov]
Subject: Perchlorate Peer Review - Final Attachments for Thursday's Meeting on the Selection Report
Attachments: TO 2015-22 Proposed Reviewer Selection Report.pdf; TO 2015-22 CV NOM 001.doc; TO 2015-22 CV NOM 002.pdf; TO 2015-22 CV NOM 007.docx; TO 2015-22 CV NOM 008.docx; TO 2015-22 CV Reviewer 02.pdf; TO 2015-22 CV Reviewer 03.pdf; TO 2015-22 CV Reviewer 07.doc; TO 2015-22 CV Reviewer 08.pdf; TO 2015-22 CV Reviewer 10.DOC; TO 2015-22 CV Reviewer 12.docx; TO 2015-22 CV Reviewer 13.docx; TO 2015-22 CV Reviewer 15.doc

The peer review selection report attached has some very minor changes from the draft report. The draft report we sent previously was distributed before the close of the comment period to allow adequate advance time for review. One comment was received at the very end of the comment period, but it does not provide any comments specific to any individuals listed as interim reviewers. The document has been updated to acknowledge that one comment. It also incorporates all the appendices into one document. There are no other changes of any substance.

I'm also attaching the CV's of the reviewers in case anyone wants to look at that level of detail.

Thanks,
Russ

Russ Perkinson
U.S. Environmental Protection Agency
Office of Ground Water and Drinking Water
1200 Pennsylvania Ave., NW
Mail Code 4607M
Washington, DC 20460
perkinson.russ@epa.gov
Phone: (202) 564-4901

Message

From: Perkinson, Russ [Perkinson.Russ@epa.gov]
Sent: 10/20/2016 12:25:10 PM
To: O'Farrell, Thomas [OFarrell.Thomas@epa.gov]
CC: Greene, Mary [greene.mary@epa.gov]; Grifo, Francesca [Grifo.Francesca@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]; Olson, Daniel [Olson.Daniel@epa.gov]
Subject: Perchlorate BBDR Model Peer Review Selection Report
Attachments: TO 2015-22 Draft Reviewer Selection Report to EPA 10.19.16.pdf; Appendix D Biosketches 10.19.16.pdf; Appendix C Reviewer Information 10.19.16.pdf; Appendix B COI Certification Letter 10.19.16.pdf

Tom – I've reviewed this selection report prepared by the contractor for the perchlorate BBDR model peer review and find it acceptable for distribution to the meeting attendees. Be advised that the comment period on the list of interim peer reviewers runs through October 21. Since you need the materials now (in advance of the comment close date) to provide adequate time for review, I instructed the contractor to place a "draft" mark on the document. If there are comments received before the end of the comment period, it is possible that some modifications will be needed. We will make you aware of any changes, if needed, early next week.

From your email yesterday, I'm assuming you or others in your office will attach the documents to the calendar entry for the meeting or otherwise will distribute to the total list of meeting attendees. If you want me to send it to the whole list, Please let me know. I'm just copying Mary and Francesca per your instructions along with my branch chief and the perchlorate team lead. **Since you indicate you are in a meeting today, I'd appreciate it if Mary or Francesca reply to me this morning if I am to distribute it to all attendees.**

Since an exact date has not been selected for the panel meeting and due to the range in expertise we are seeking, I asked the contractor to provide eight names for the final panel along with several alternates having varied expertise (primarily in the event that the precise date selected conflicts with a reviewer's availability).

Regards,
Russ

Russ Perkinson
U.S. Environmental Protection Agency
Office of Ground Water and Drinking Water
1200 Pennsylvania Ave., NW
Mail Code 4607M
Washington, DC 20460
perkinson.russ@epa.gov
Phone: (202) 564-4901

References

Clewell RA, Merrill EA, Gearhart JM, Robinson PJ, Sterner TR, Mattie DR, et al. 2007. Perchlorate and radioiodide kinetics across life stages in the human: using PBPK models to predict dosimetry and thyroid inhibition and sensitive subpopulations based on developmental stage. J Toxicol Environ Health A 70:408-428.

Fisher JW, Li S, Crofton K, Zoeller RT, McLanahan ED, Lumen A, et al. 2013. Evaluation of Iodide Deficiency in the Lactating Rat and Pup Using a Biologically Based Dose-Response Model. Toxicol Sci 132:75-86.

Lumen A, Mattie DR, Fisher JW. 2013. Evaluation of Perturbations in Serum Thyroid Hormones During Human Pregnancy Due to Dietary Iodide and Perchlorate Exposure Using a Biologically Based Dose-Response Model. Toxicol Sci 133:320-341.

NRC. 2005. Health Implications of Perchlorate Ingestion. U.S. National Research Council, National Academies Press, Washington, D.C. Available at: [HYPERLINK "https://www.nap.edu/catalog/11202/health-implications-of-perchlorate-ingestion."].

Schlosser P, Leavens T, Ramasamy S. 2016. Biologically Based Dose Response Models for the Effect of Perchlorate on Thyroid Hormones in the Infant, Breast Feeding Mother, Pregnant Mother, and Fetus: Model Development, Revision, and Preliminary Dose-Response Analyses [Public Review Draft]. Other Contributors: Fisher, J.; Lumen, A.; McLanahan, E. Available at: [HYPERLINK "https://www.regulations.gov/document?D=EPA-HQ-OW-2016-0438-0002"].

U.S. EPA. 2009. Inhibition of the sodium-iodide symporter by perchlorate: An evaluation of life stage sensitivity using physiologically based pharmacokinetic (PBPK) modeling. U.S. Environmental Protection Agency, Office of Research and Development, EPA/600/R-08/106A, May 2009. Available at: [HYPERLINK "https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=212508&CFID=80937054&CFTOKEN=35291271"].

U.S. EPA. 2012. White paper: Life stage considerations and interpretation of recent epidemiological evidence to develop a maximum contaminant level goal for perchlorates. U.S. Environmental Protection Agency, Office of Water, Office of Science and Technology, Health and Ecological Criteria Division. Available at: [HYPERLINK "https://yosemite.epa.gov/sab/sabproduct.nsf/0/D3BB75D4297CA4698525794300522ACE/$File/Final+Perchlorate+White+Paper+05.29.12.pdf"].

U.S. EPA. 2013. SAB advice on approaches to derive a maximum contaminant level goal for perchlorate, U.S. Environmental Protection Agency, Science Advisory Board, EPA/SAB/13/004. Available at: [HYPERLINK "https://www.epa.gov/dwstandardsregulations/perchlorate"].

Message

From: Townsend, Clifton [Townsend.Clifton@epa.gov]
Sent: 10/13/2016 2:19:59 PM
To: Kyprianou, Rose [Kyprianou.Rose@epa.gov]; Christ, Lisa [Christ.Lisa@epa.gov]
Subject: RE: AWWA Reference 2009
Attachments: HypochloriteAssess.pdf

Hi Rose,

Attached is the reference that I sent earlier from AWWA and Water Research Foundation.

Clifton

From: Kyprianou, Rose
Sent: Thursday, October 13, 2016 8:36 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>; Townsend, Clifton <Townsend.Clifton@epa.gov>
Subject: RE: AWWA Reference 2009

Looping in Clifton.

Rose Kyprianou
Acting Chief, Regulatory Management Branch II
EPA/OPP/AD
Phone: (703)-305-5354, Office: S-8622

From: Christ, Lisa
Sent: Thursday, October 13, 2016 8:33 AM
To: Kyprianou, Rose <Kyprianou.Rose@epa.gov>
Subject: RE: AWWA Reference 2009

Hey Clif – I get an error when I try to access the report. Also, did you send the regdet FRN to Rose?
Thnx-Lisa

From: Kyprianou, Rose
Sent: Wednesday, October 12, 2016 4:28 PM
To: Townsend, Clifton <Townsend.Clifton@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: AWWA Reference 2009

Thanks so much for your time and these email references, and very nice to talk with you both again. We'll be in touch with any other questions and an update of where we think we are coming out.

Rose

Rose Kyprianou
Acting Chief, Regulatory Management Branch II

EPA/OPP/AD
Phone: (703)-305-5354, Office: S-8622

From: Townsend, Clifton
Sent: Tuesday, October 11, 2016 3:26 PM
To: Kyprianou, Rose <Kyprianou.Rose@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: AWWA Reference 2009

Hi Rose,

Below is the AWWA reference that we talked about it in the meeting.

Clifton

American Water Works Association (AWWA) and Water Research Foundation (WaterRf). 2009. *Hypochlorite – An Assessment of Factors That Influence the Formation of Perchlorate and Other Contaminants*. Available on the Internet at: http://www.awwa.org/files/GovtPublicAffairs/PDF/HypochloriteAssess.pdf

Clifton C. Townsend, MSPH
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U.S. Environmental Protection Agency
Office of Ground Water and Drinking Water
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E-mail: townsend.clifton@epa.gov

HYPOCHLORITE—

An Assessment of Factors That Influence the Formation of Perchlorate and Other Contaminants

Jointly Funded by

American Water Works Association

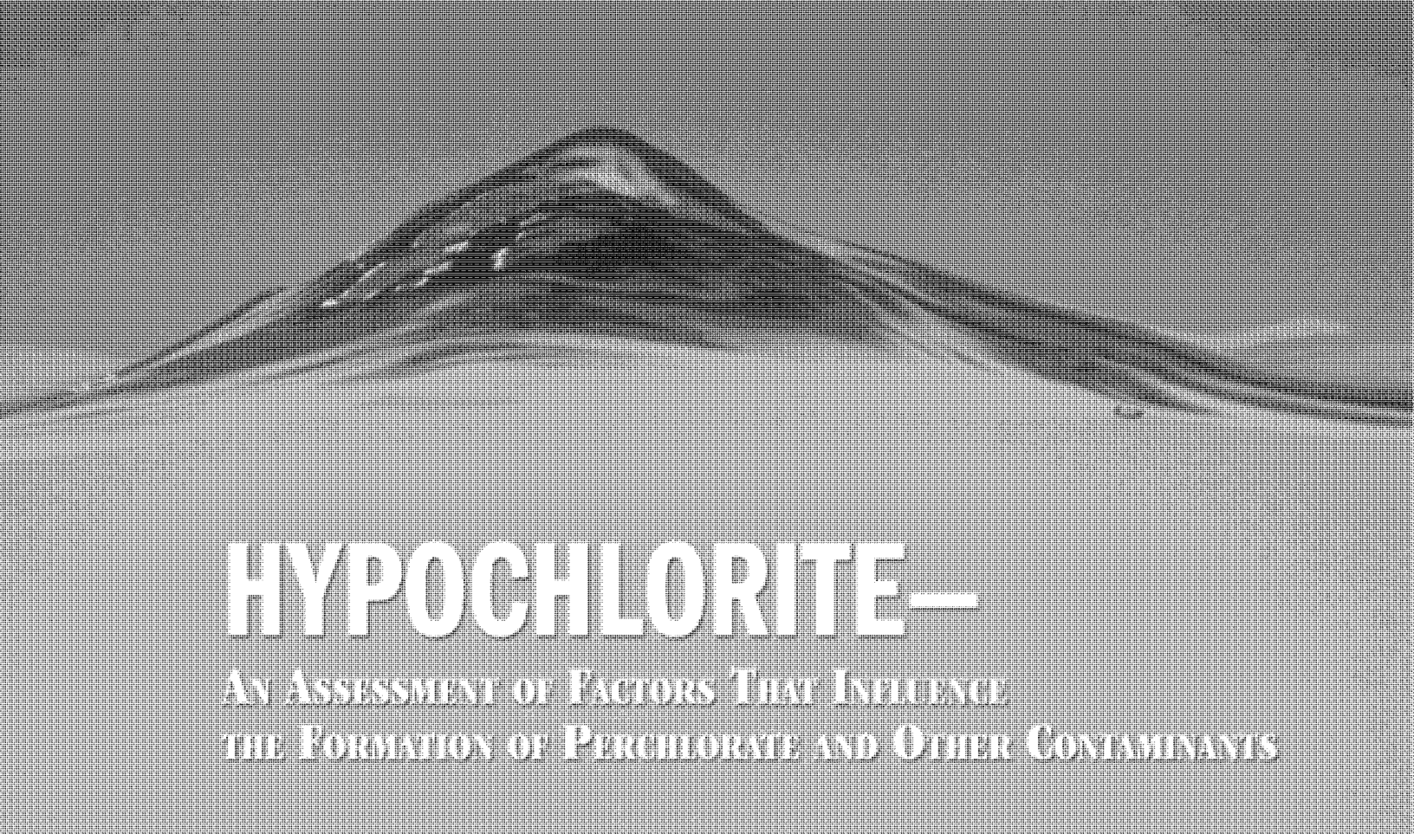
WATER RESEARCH FOUNDATION

Advancing the Science of Water

Disclaimer

This study was jointly funded by American Water Works Association's Water Industry Technical Action Fund and the Water Research Foundation. These entities assume no responsibility for the content of the research study reported in this publication or the opinions or statements of fact expressed in this report. The mention of trade names for commercial products does not represent or imply the approval or endorsement of AWWA or Water Research Foundation. This report is presented solely for informative purposes.

American Water Works Association
6666 West Quincy Avenue
Denver, Colorado 80235



HYPOCHLORITE—

An Assessment of Factors That Influence the Formation of Perchlorate and Other Contaminants

Prepared by:
Shane A. Snyder, Benjamin D. Stanford, and Aleksey N. Pisarenko
Southern Nevada Water Authority
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Las Vegas, NV 89193-9954

And

Gilbert Gordon
Miami University
Department of Chemistry and Biochemistry,
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National Institute of Public Health, Japan

Jointly Funded by:
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Water Industry Technical Action Fund

And

Water Research Foundation

Published by the American Water Works Association

American Water Works Association

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CONTENTS

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TABLES

FIGURES

American Water Works Association is the authoritative resource for knowledge, information and advocacy to improve the quality and supply of water in North America and beyond. AWWA is the largest organization of water professionals in the world. AWWA advances public health, safety and welfare by uniting the efforts of the full spectrum of the entire water community. Through our collective strength we become better stewards of water for the greatest good of the people and the environment.

The Water Research Foundation (formerly Awwa Research Foundation) is a member-supported, international, nonprofit organization that sponsors research to enable water utilities, public health agencies, and other professionals to provide safe and affordable drinking water to consumers.

Water Industry Technical Action Fund (WITAF) is administered by AWWA and is funded through member dues. WITAF funds information collection and analysis and other activities in support of sound and effective legislation, regulation, and drinking water policies and programs.

ACKNOWLEDGMENTS

This report was funded by the American Water Works Association, Water Industry Technical Action Fund (WITAF) and the Water Research Foundation. The research team greatly appreciates the diligent efforts of the Southern Nevada Water Authority's (SNWA) Applied R&D Center (ARDC). Specifically, we wish to acknowledge Oscar Quiñones, Brett Vanderford, Doug Mawhinney, and Beck Trenholm for their assistance with the development and troubleshooting of the analytical methods employed throughout this project. In addition, we would like to thank Shanon Fergusson, Elaine Go, Christy Meza, Josephine Chu, and Janie Zeigler for assistance with the sample handling and preparation. We also wish to thank David Rexing, Linda Parker, and Ron Zegers for their support and assistance through the project.

The research team would like to acknowledge Kevin M. Morley of the American Water Works Association and Alice Fulmer of the Water Research Foundation for their relentless leadership and guidance throughout the project. The team also wishes to thank the Project Advisory Committee members for their thoughtful insight and careful review of our project reports:

Gary Lynch, Park Water Company
Robert Cushing, Carollo Engineers
Andrew Eaton, MWH Laboratories
Gary Emmert, University of Memphis
Richard Sakaji, East Bay MUD

The team is especially appreciative of the support of the participating manufacturers and utilities for providing water samples, hypochlorite samples, and information regarding equipment and operations:

MIOX Corporation
Severn Trent Services
Arch Chemical

EXECUTIVE SUMMARY

INTRODUCTION

The use of chlorine for the disinfection of water has arguably saved more human lives than any other public health action in history, with a legacy dating back over 150 years. Since chlorine's first use in 1846 at a hosipital in Vienna, Austria to prevent the spread of "child bed fever", many applications of the chemical have been explored including the first full scale chlorine installation for drinking water disinfection in Chicago in 1908. During the 100 years since its use in drinking water disinfection, chlorination and filtration of drinking water has been estimated to be responsible for a 50% increase in life expectancy. Today, 98% of North American community water treatment systems use chlorine for disinfection[1],[2].

Sodium hypochlorite is a commonly used form of chlorine in drinking water and water reuse applications for its ability to disinfect and maintain a residual level of disinfectant throughout the distribution system. Approximately 1/3 of all drinking water treatment plants (DWTPs) in the United States use bulk hypochlorite for disinfection. Though the majority of liquid hypochlorite use is in the form of bulk hypochlorite delivered from regional manufacturers and/or destributors, around 8% of US DWTPs use on-site hypochlorite generators (OSG). Additionally, due to security concerns associated with chlorine gas use, additional utilities may opt or be required to switch from their current disinfection practices to bulk or OSG hypochlorite.

Hypochlorite is known to contain various impurities, including bromate, chlorate, and chlorite. These contaminants may be present during manufacturing and/or may form during transport and storage. Recently, perchlorate has been detected at elevated levels in hypochlorite solutions. Considering that perchlorate is under consideration for Federal regulation and is currently regulated in California, New Jersey, and Massachusettes[3], it is critical that contribution of perchlorate from hypochlorite solutions be quantified. Bromate is another contaminant of hypochlorite solutions that may impact drinking water quality. Although bromate is regulated by a primary enforcable standard under the Safe Drinking Water Act, the regulated level could be lowered during the 6-year review process.

With these considerations in mind, our research team developed a plan to investigate the factors impacting the formation of perchlorate, bromate, and other contaminants in hypochlorite solutions and to develop a set of guidelines to assist utilities in minimizing the formation of such contaminants. Our project objectives also included the development of a detailed chemical rate law from which predictions could be made reagarding the formation of perchlorate in a given bulk hypochlorite solution.

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[1] White, G.C. The Handbook of Chlorination, 2nd Ed. Von Nostrand Reinhold. New York, 1986.

[2] Leidholdt, R. Chlorine - "Special Agent" for Disinfecting Water. American Water Works Association. Vol. 26. No. 6. pp 40-43. June 2000.

[3] CA MCL = 6 µg/L; NJ MCL = 5 µg/L; MA MCL = 2 µg/L

RESEARCH OBJECTIVES

Based upon conversations with the Water Research Foundation Project Advisory Committee (PAC) and in accordance with specific objectives from within the AWWA RFP, the Project Team identified the following primary research objectives designed to provide the data necessary to determine the mechanisms, and to develop a predictive model, for perchlorate formation in hypochlorite solutions:

1. Determine the analytical method(s) most appropriate for measurement of oxyhalide anions in bulk hypochlorite solutions, OSG solutions, and utility water samples.

2. Determine the impact of co-occurring oxyhalide anions on the formation of perchlorate.

3. Determine the impact of pH, ionic strength, transition metals, and temperature on perchlorate formation.

4. Determine the detailed chemical rate law to predict perchlorate formation in hypochlorite solutions.

Additional secondary objectives were also developed to address concerns regarding operational considerations (i.e., hypochlorite sources, on-site generation, and other factors):

5. Compare perchlorate concentrations in bulk hypochlorite and different OSG systems, including those operated in mixed oxidant mode.

6. Determine the contribution of perchlorate in finished waters originating from hypochlorite addition.

7. Provide recommendations for water utilities to minimize the presence of perchlorate, bromate, chlorate, and chlorite in hypochlorite solutions.

RESEARCH APPROACH

In order to address the objectives outlined above, the Project Team designed a four-tiered approach to completing the project in less than one year. The specific tasks from the research approach were as follows:

Task 1: Comprehensive Literature Review
Task 2: Analysis of Impurities in Hypochlorite
Subtask 2.1: Perchlorate in Commercially Available Hypochlorite
Subtask 2.2: Impact of transition metals on perchlorate formation
Subtask 2.3: Determination of Factors Related to Perchlorate Formation and Minimization in Hypochlorite
Task 3: Treatment/Manufacturing System Impact on Drinking Water
Task 4: Recommendations and Final Report

These tasks are discussed in detail in Chapter 1 of this report. In short, a detailed (though dynamic) experimental matrix was designed to test how variables such as hypochlorite concentration, chlorate concentration, ionic strength, bromide and/or bromate, transition metal ions, pH, and temperature would impact the rate of perchlorate formation. Most of the initial experiments were designed to be run at elevated temperatures (60 °C) in order to provide rapid feedback regarding the impact of individual variables of perchlorate formation. In this manner, short incubation studies (e.g., 15 to 30 days) were used to design follow-up experiments at lower temperatures (thus longer incubation times of up to 200 days) targeting specific variables likely to have the most effect on perchlorate formation. In total, over 5000 data points were collected. These data were used to validate methods, elucidate the mechanism of perchlorate formation, build a detailed chemical rate law, and to validate the rate law on utility and OSG hypochlorite samples. Seven water treatment utilities, two OSG manufacturers, and one calcium hypochlorite supplier participated in this study, providing samples from five different bulk hypochlorite suppliers, 12 OSG systems, and one solid calcium hypochlorite sample.

REPORT OVERVIEW

This Final Report is divided into 6 Chapters, each of which is designed to carry the reader through the scientific process behind developing the "Predictive Model" and the specific recommendations for minimizing the formation of perchlorate in stored hypochlorite solutions.

- Chapter 1 contains background information on occurrence, regulation, and hypothesized mechanisms of formation for perchlorate and other regulated and non-regulated contaminants of hypochlorite solutions. This Chapter also provides a context for the current study and outlines the research approach in detail.

- Chapter 2 describes the development of analytical methods and subsequent validation of analytical methods used for the identification and quantification of perchlorate, chlorate, and bromate within concentrated hypochlorite solutions. This chapter also provides methodologies applied for other contaminants previously identified in hypochlorite.

- Chapter 3 examines the factors which influence the rate of perchlorate formation in hypochlorite solutions. Key factors identified include, hypochlorite ion concentration, chlorate ion concentration, ionic strength, and temperature.

- Chapter 4 describes the development and validation of the detailed chemical rate law which is applied for predicting the concentration of perchlorate in a given bulk hypochlorite solution.

- Chapter 5 provides the results of a survey of bulk and OSG hypochlorite solutions obtained from various manufactures and facilities for perchlorate, chlorate, and bromate. This chapter also provides the application of the rate law to predict perchlorate concentration in hypochlorite.

- Chapter 6 summarizes the findings of the study and provides recommendations to utilities on how to minimize the formation of perchlorate in bulk hypochlorite.

CONCLUSIONS

Robust analytical techniques were developed to determine the concentration of perchlorate, chlorate, and bromate in concentrated hypochlorite solutions. An LC-MS/MS method was used for all perchlorate and bromate analyses. Both LC-MS/MS and titration methods were successful for chlorate analysis; however, LC-MS/MS was found to be more robust in hypochlorite solutions with free available chlorine (FAC) < 5%, while titration was found to be superior in hypochlorite solutions containing > 5% FAC.

The formation of perchlorate occurs over time as hypochlorite degrades, while bromate is rapidly formed during hypochlorite manufacturing and does not change significantly over time. The formation of perchlorate is impacted by several key factors including:

- Direct factors such as hypochlorite and chlorate concentration, ionic strength, and pH
- Indirect factors such as metal ions and bromide concentration
- Environmental factors such as temperature

Considering the variables and experimental boundaries described in this report, perchlorate formation was found to be first order in both hypochlorite and chlorate ion concentration and is highly dependent upon ionic strength and temperature. These factors were used to develop a predictive model for perchlorate that was found to agree within 10% of measured values within the boundary conditions established in this study (i.e., pH 11 – 13 and temperatures to 50° C). It should be noted, however, that in order to validate a predictive model at any temperature, a minimum of at least 1.5 half-lives are required. For the perchlorate predictive model at temperatures below 30 °C, the time required to reach at least 1.5 half-lives would have exceeded the time allotted for the study. Thus, while the model has been validated between 30 °C and 50 °C, any information gathered from lower temperatures should be limited to qualitative information only until low-temperature studies can be completed.

Finally, a set of 5 bulk hypochlorite solutions, 12 OSG hypochlorite solutions, and one calcium hypochlorite sample was obtained for contaminant analysis and quantification and was used in a holding study to examine the rate of perchlorate formation in each solution. All samples tested had measurable concentrations of chlorate, perchlorate, and bromate. No specific conclusions could be made regarding differences in contaminant concentrations in bulk, OSG, and calcium hypochlorite solutions. There did appear to be, however, a link between salt quality and bromate concentration in OSG samples, suggesting that a salt of a higher purity (in this study, >99.5% as NaCl) may be useful for reducing the amount of bromate in the hypochlorite product. However, this trend needs to be further investigated before a specific recommendation on salt purity and maximum levels of bromide can be quantified. When the various solutions were aged, good correlation was observed between the rate of perchlorate formation, the concentration of hypochlorite and chlorate ions, and ionic strength. Furthermore, the "Predictive Model" was able to predict perchlorate formation in the bulk hypochlorite samples to within 20% of the measured concentration for up to 28 days at 50 °C.

RECOMMENDATIONS

Based on the findings presented in this report, several key factors have been identified that impact the formation of perchlorate, bromate, and other contaminants in hypochlorite solutions. The major factors impacting perchlorate formation parallel those previously described for reducing the decomposition of hypochlorite: temperature, ionic strength, concentration, and pH. By using the information gathered during this study and by applying the "Predictive Model" to hypothetical liquid hypochlorite storage scenarios, several quantitative and qualitative recommendations can be made:

a. Dilute stored hypochlorite solutions upon delivery: The decomposition of hypochlorite and subsequent formation of chlorate and perchlorate is dependent upon hypochlorite concentration and ionic strength. Higher ionic strength and hypochlorite concentration will drive the reaction towards a greater production of chlorate and perchlorate while also increasing the rate of decomposition of hypochlorite. By diluting a 2 molar hypochlorite solution by a factor of 2, the rate of perchlorate formation decreases by a factor of 7 due to the combination of concentration and ionic strength effects. A four-fold dilution of a hypochlorite solution will decrease the rate of formation by 36. A ten-fold dilution of a hypochlorite solution will decrease the rate of perchlorate formation by a factor of 270.

b. Store the hypochlorite solutions at lower temperatures: Higher temperatures speed up the chemical decomposition of hypochlorite and the subsequent formation of chlorate and perchlorate. Every 5 °C reduction in storage temperature will reduce the rate of perchlorate formation by a factor of approximately 2.

c. Control the pH of stored hypochlorite solutions at pH 11 – 13, even after dilution: Storage of concentrated hypochlorite solutions at pH values lower than 11 is not recommended due to rapid decomposition of hypochlorite ion/hypochlorous acid and the consequent formation of chlorate even though this reduces the amount of perchlorate formed. When the pH is higher than 13, perchlorate formation is enhanced due to the ionic strength effect. As such, utilities should continue to insist that manufacturer specifications include pH control in the range of 11 to 13. Given the typical pH range of OSG hypochlorite (pH 9 to 10), such solutions should be used as soon as possible after manufacture and should not be stored for more than 1-2 days.

d. Control the removal of transition metal ions by purchasing filtered hypochlorite solutions and by using low-metal ion concentration feed water for the OSG systems: The presence of transition metal ions results in an increased degradation rate of hypochlorite. While this degradation is concomitant with reduced perchlorate formation, the FAC concentration is also reduced, forcing a utility to use a higher volume of a hypochlorite solution which results in higher mass loading of contaminants such as perchlorate, chlorate, and bromate.

e. Use fresh hypochlorite solutions when possible: Over time, hypochlorite will naturally decompose to produce oxygen, chlorate, and perchlorate. Less storage time

will minimize the formation of these contaminants in the hypochlorite solution. A fresh hypochlorite solution will also contain a higher concentration of hypochlorite, thereby reducing the amount of solution required to obtain the target chlorine residual. Again, higher hypochlorite concentration in a fresh hypochlorite solution will correspond to lower concentrations of contaminants dosed.

f. For utilities using OSG hypochlorite, use low-bromide salt to minimize the amount of bromide present in the brine: Bromate formation will occur rapidly in hypochlorite solutions in the presence of bromide. By controlling the amount of bromide in the salt and source water used for on-site generation, bromate formation can be minimized.

If a utility were to combine dilution with temperature reduction, a significant impact on hypochlorite decomposition and perchlorate formation would be observed. For example, as described in Chapter 4 if a utility were to dilute a 13% bulk hypochlorite solution by a factor of 2 and also reduce the storage temperature by 10 °C, the result would be 16 times less hypochlorite decomposition and 27 times less perchlorate formation than if the hypochlorite were stored at ambient temperatures undiluted. Chapter 4, Table 4.8 details the combined effects of temperature and dilution for various storage scenarios.

Another interpretation of the results of this study is through seasonal trends. If, for example, a utility experienced average bulk hypochlorite storage temperatures of 10 °C in the winter and 35 °C in the summer, the rate of perchlorate formation for 13% hypochlorite would be nearly 18 times faster in the summer. In other words, in winter that utility could expect the concentration of perchlorate concentration to increase by a factor of 10 in approximately 3 months; in summer it would increase by a factor of 10 in only 5 days. Had the hypochlorite solution been diluted by a factor of 2, the same increase in perchlorate concentration would take one month in summer and 20 months (assuming, for example, an average temperature of 10 °C) in winter. Therefore, in order to minimize the amount of perchlorate formation in hypochlorite solutions, a combination of dilution and temperature control is recommended.

QUESTIONS FOR UTILITIES TO ASK BULK HYPOCHLORITE AND OSG SUPPLIERS

Based upon the findings of this study, a series of questions have been developed to assist utilities in developing questions that they may wish to ask hypochlorite manufacturers. While these questions are not meant to preclude or give advantage to any manufacturer or process, they are meant to help utilities obtain the information that might be of use to them in deciding how to store and handle the hypochlorite solutions that they purchase or produce on-site.

Questions for Bulk Hypochlorite Manufacturers

1. What is the temperature of the hypochlorite solution directly after manufacture?
2. At what temperature is the hypochlorite solution stored between manufacture and delivery?
3. Is there a cooling system in place to lower the temperature of the final product at the manufacturing facility?
4. Do the delivery vehicles have any cooling systems in place to hold the hypochlorite solution at a constant temperature during transport?

5. What is the concentration of hypochlorite at the time of delivery? If unknown, can the manufacturer provide the concentration of hypochlorite at the time of manufacture together with the age and storage conditions of the hypochlorite solution?
6. Do they know the concentration of bromate, chlorate, and perchlorate in the hypochlorite solutions? If so, will they provide that information?
7. What is the ionic strength of the hypochlorite solution at the time of manufacture? Does the manufacturer offer any means to reduce the ionic strength?
8. What quality of salt is used during the manufacturing process? How much bromide is present in the salt?
9. What is the concentration of transition metals (nickel, manganese, iron, cobalt, and copper) are present in the hypochlorite solution? Do these values fall within the NSF specifications for metals?
10. Does the manufacturer offer filtered hypochlorite solutions?

Questions for On-Site Generator Manufacturers

1. Does the OSG manufacturer have any specific recommendations about quality or source of salt?
2. Do they know of any specific impurities in salt that can adversely impact OSG operation or formation of contaminants in the hypochlorite solution product?
3. Does the OSG manufacturer know the range of perchlorate concentration in the final OSG solution for their various models?

Questions for Salt Suppliers

1. What is the source of the salt being delivered?
2. What is the purity (as NaCl) of the salt delivered?
3. What is the concentration of bromide in the salt?
4. What concentration of transition metals (nickel, manganese, iron, cobalt, and copper) is present in the salt?

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CHAPTER 1
INTRODUCTION

BACKGROUND

Sodium hypochlorite (a.k.a. "bleach") is commonly used in drinking water and water reuse applications for its ability to disinfect and maintain a residual level of disinfectant throughout the distribution system. Multiple regulated contaminants exist in hypochlorite solutions including bromate, hypochlorite itself, and chlorite (Gordon, Pacey, and Bubnis 1993; Weinberg, Delcomyn, and Unnam 2003; Chlorine_Institute 2004; Asami, Kosaka, and Kunikane 2009) in addition to other unregulated oxyhalides such as chlorate and perchlorate. The presence of such oxyhalides in drinking water has become a major issue of concern for the water industry. Recently, perchlorate has been identified as a contaminant of concern in hypochlorite solutions and has received a large amount of attention as it is an endocrine disrupting compound which can impact the thyroid system of humans (Lamm, et al. 1999; Urbansky 2000a; York, et al. 2001; Greer, et al. 2002b).

Perchlorate is both a natural and anthropogenic compound: perchlorate has been found to occur naturally in the US and Chile (Dafert 1908; Jackson, et al. 2005) and has also been manufactured and used as an oxidizer for solid fuel engines, fireworks, and road flares (Davis 1940; Hampel and Leppla 1947; Simchen and Inbar-Rozem 1968; Urbansky 2000a). Chilean nitrate, a source of naturally occurring perchlorate, has been used for many years in agricultural applications in the United States. Where large quantities of perchlorate have been produced or used, perchlorate contamination of soil and water has been detected, with concentrations approaching 3,000 mg/L at former industrial sites in the Las Vegas valley. Modern analytical instrumentation has facilitated the detection of perchlorate in drinking water, dairy products, human breast milk, plants, fish, and cattle (Urbansky, et al. 2000b; Kirk, et al. 2003; Sundberg, et al. 2003; Cheng, et al. 2004; Dodds, et al. 2004; Yu, et al. 2004; Kirk, et al. 2005; Sanchez, et al. 2005; Snyder, Vanderford, and Rexing 2005). Perchlorate has also been detected in kelp (Orris, et al. 2003; Martinelango, Tian, and Dasgupta 2006), which is often used as a source of iodine in dietary supplements (Turrentine 1924; Teas, et al. 2004).

In 2002 the US EPA published a reference dose (RfD) for perchlorate of 0.00003 mg/kg/day, which would suggest drinking water equivalent level (DWEL) of approximately 1 µg/L (USEPA 2002; Tiemann 2008). In 2005 the National Academy of Sciences and the US EPA updated the RfD to 0.0007 mg/kg/day with a DWEL of 24.5 µg/L (USEPA 2006), a number based on the no observable effect level (NOEL) of 0.007 mg/kg-day for inhibition of iodide uptake determined in a human clinical trial (Greer, et al. 2002a). Despite coming forward with an updated RfD, it is unclear whether or not perchlorate will be regulated nationally at this time (Swackhamer and Rose 2008; Tiemann 2008). However, the state of Massachusetts has set a DWEL and maximum contaminant level (MCL) of 2.0 µg/L for perchlorate (MA_DEP 2006), and California has established a MCL of 6.0 µg/L (CA_DPH 2007). Based on data from this study and data published elsewhere, perchlorate appears to be a ubiquitous contaminant of hypochlorite solutions and the perchlorate concentration in hypochlorite increases significantly over time (Greiner, et al. 2008; Asami, Kosaka, and Kunikane 2009).

Chlorate is a contaminant produced during on-site generation of hypochlorite solutions and the subsequent decomposition of hypochlorite. Chlorate is also a by-product of treatment of drinking water with chlorine dioxide (USEPA 1999; Snyder, Vanderford, and Rexing 2005).

Toxicological reports have shown that chlorate has similar toxic modes of action as the unregulated contaminant perchlorate. The state of California has set an action level for chlorate in drinking water of 800 µg/l (Drinking Water Notification Levels 2004); an action level as low as 200 µg/l has been suggested (Howd 2002). The World Health Organization has set a guideline MCL of 700 µg/L (WHO 2008). Chlorate exhibits the same mechanism of action on the thyroid as perchlorate, albeit with lower potency (USEPA 1999; Pleus 2000; Hooth, et al. 2001). Chlorate has been shown to occur in bottled water and in municipal drinking water at levels up to 270 µg/l (Snyder, Vanderford, and Rexing 2005). Chlorate occurs in drinking waters at levels much greater than those reported for perchlorate, thus, even though it is less potent than perchlorate, its toxicological relevance and occurrence is significant in holistic exposure assessments of goitrogens.

Bromate is another possible contaminant of hypochlorite solutions (Asami, Kosaka, and Kunikane 2009) and results from the oxidation of bromide to hypobromite to bromate via a mechanism analogous to that of chlorate. Bromate may also form during ozonation when bromide is oxidized by dissolved ozone in water. Bromate has been reported to be a carcinogen in mammalian studies (Kurokawa, et al. 1986; DeAngelo, et al. 1998) and is suspected to have a role in oxidative DNA damage in target organs (Ballmaier and Epe 1995; Chipman, et al. 1998). Bromate is currently regulated by the US EPA in drinking water at an MCL of 10 µg/L and is specified in hypochlorite solutions not to exceed 0.5 µg BrO_3^-/mg FAC (NSF/ANSI 2005).

Given the high likelihood of finding perchlorate (in addition to chlorate, chlorite, and bromate) in hypochlorite solutions and the widespread use of hypochlorite, the potential contribution of perchlorate from hypochlorite is a critical issue to understand. To exacerbate this situation, some utilities that once used gaseous chlorine are moving to the use of hypochlorite solutions due to homeland security concerns related to chlorine gas. The potential health impacts of perchlorate have been widely debated in the public media, and it is likely that additional states will begin to regulate perchlorate in drinking water independent of any US EPA regulatory determinations. Thus, it is vital that the water industry has the predictive tools available to understand how much perchlorate is added to drinking waters from hypochlorite and what measures can be taken to minimize the formation of perchlorate in hypochlorite solutions.

BULK HYPOCHLORITE MANUFACTURING AND USE IN DRINKING WATER TREATMENT

Of the drinking water treatment plants (DWTPs) in the United States, approximately 31% use bulk hypochlorite solutions for disinfection and 63% use chlorine gas (Routt 2008; Routt, et al. 2008). Additionally, 8% of US DWTPs use on-site generators (OSGs) for electrolytical sodium hypochlorite production from brine solutions and 8% use calcium hypochlorite (note that utilities may use more than one process for disinfection, thus numbers do not total 100%). There are multiple suppliers with multiple configurations of OSG systems including MIOX Corporation, Severn Trent (ClorTec), US Filter, and others and there are equally as many suppliers of bulk hypochlorite. It is generally manufactured by passing chlorine gas through sodium hydroxide. Sodium hydroxide is frequently produced by means of the chlor-alkali process, in which an aqueous sodium chloride solution is electrolyzed to produce chlorine gas and sodium hydroxide (Gordon, et al. 1993; Gordon, Pacey, and Bubnis 1993; Gordon, Adam, and Bubnis 1994; Gordon, Adam, and Bubnis 1995). In this context it should be noted that there are only five remaining chlor-alkali mercury cell systems still manufacturing sodium hydroxide

in the United States (Oceana 2007). However, unlike the myriad configurations for OSGs, the majority of bulk hypochlorite suppliers utilize either a Powell Fabrication Generator and/or batch process. OSGs, on the other hand, vary much more widely in terms of the chemical composition of electrode materials, energy inputs, configuration, feed water quality, and salt quality. Different OSGs also have inter- and intra- brand differences. Thus, bulk hypochlorite tends to be more uniform in quality and production methods than OSG hypochlorite. Another major difference between bulk hypochlorite and OSG hypochlorite is in the concentration of hypochlorite produced: bulk hypochlorite is typically delivered as a 13% hypochlorite solution while OSG hypochlorite ranges from less than 1 % free available chlorine (FAC) to 4 % FAC.

Other sources of chlorine are available to DWTPs including calcium hypochlorite, chlorine gas, and chlorine dioxide. Calcium hypochlorite (in solid form) should, theoreticaly, have a longer shelf life than liquid hypochlorite as the decomposition of hypochlorite requires an aqueous solution. However, calcium hypochlorite is typically used only as an emergency back-up process or in small-scale operations due to increased maintenance and water hardness issues associated with its use. Chlorine dioxide is another alternative to hypochlorite which has been shown to help reduce the formation of trihalomethanes (THMs) though may be associated with increased chlorite concentration in finished water (McGuire, Lieu, and Pearthree 1999). Chlorine gas is another popular option for disinfection of drinking water and is currently used by approximately 60% of DWTPs in the United States. Because of the low concentration of dissolved chlorine gas, appreciable quantitites of perchlorate, chlorate, and chlorite are not expected to form. There are, however safety and security issues associated with handling, storage, and application. Thus, many utilities currently using chlorine gas are considering the implications of switching to the use of hypochlorite, both from a cost perspective and from a contaminant perspective.

REGULATED AND UNREGULATED CONTAMINANTS OF HYPOCHLORITE SOLUTIONS

With the differences in concentration and production processes associated with hypochlorite solutions is a concomitant difference associated with the presence and formation of contaminants. For example, small quantities of transition metal ions such as nickel(II), copper(II), manganese(II), cobalt(II) and iron(III) may be present in unfiltered finished hypochlorite solutions. Small concentrations of these ions (on the order of 1 to 2 mg/L) have been shown increase the rate of decomposition of hypochlorite by as much as 1 to 2 orders of magnitude (Gordon, Adam, and Bubnis 1994; Gordon, Adam, and Bubnis 1995) and have been hypothesized to play a catalytic role in the formation of perchlorate. Interestingly, perchlorate is also produced through an electrolytic process where chlorate may be oxidized to perchlorate (Urbansky 2000a), a distinct possibility in electrolytic hypochlorite manufacturing processes. Snyder, Vandeford, and Rexing (2005) reported that perchlorate was measurable in hypochlorite originating from an on-site hypochlorite generator. The Japanese National Institute of Public Health (JNIPH) reported that as a commercially available hypochlorite solution decayed, perchlorate concentration increased (Asami, Kosaka, and Kunikane 2007). Likewise, the JNIPH also noted that perchlorate concentration was relatively low in hypochlorite solutions produced by on-site generation. Generally speaking, however, there is little additional quantitative data regarding the concentration of perchlorate in hypochlorite solutions. To the best of our knowledge, neither have any reports been published that provide hard evidence regarding the

kinetics of perchlorate formation, nor have any reports discussed ways to minimize its formation in hypochlorite.

Chlorate and chlorite, on the other hand, are well known degradation products and contaminants of hypochlorite solutions and are present in all hypochlorite (Gordon, Adam, and Bubnis 1995). Chlorate is currently unregulated at the Federal level (though the World Health Organization has set a guideline MCL of 700 µg/L) while chlorite is Federally regulated in drinking water by the US EPA with an MCL of 0.8 mg/L. Hypochlorite ion is unstable and undergoes two independent modes of self-decomposition. In one mode, oxygen and chloride are formed and in the other mode, chlorate and chloride are formed:

$$2OCl^- \rightarrow O_2 + 2Cl^- \quad \textbf{(1.1)}$$

$$3OCl^- \rightarrow ClO_3^- + 2Cl^- \quad \textbf{(1.2)}$$

The rate of decomposition of hypochlorite to form chlorate and/or oxygen is well defined in terms of the following rate law:

$$\frac{d[OCl^-]}{3dt} = k_{obs}[OCl^-]^2 \quad \textbf{(1.3)}$$

Chlorite is rapidly formed as a steady state species (not shown) in Equation 2 that serves as an intermediate between hypochlorite and chlorate. The typical half-life for decomposing 12 to 13 weight % hypochlorite (OCl^-) at room temperature (25°C) is on the order of 150 to 160 days (Gordon, et al. 1997). Changes in temperature also markedly affect the rate of decomposition of hypochlorite solutions. For example, an increase of 10 °C will increase the rate of decomposition by a factor 3.5 to 4.0. As previously mentioned, 1 to 2 mg/L of transition metal ions increase the rate of decomposition of hypochlorite by as much as 1 to 2 orders of magnitude (Gordon, Adam, and Bubnis 1994; Gordon, Adam, and Bubnis 1995), thereby impacting the formation of chlorate as well. With different types of contaminants present in hypochlorite and the specific storage conditions (e.g., temperature, pH) one reaction pathway may be favored over another, thereby potentially creating more chlorate and perchlorate in the process. Furthermore, the formation of perchlorate has been hypothesized elsewhere to be a direct result of reactions between hypochlorite and chlorate as the solution decomposes (Asami, Kosaka, and Kunikane 2007; Asami, Kosaka, and Kunikane 2009).

Bromate is another contaminant typically associated with ozonation of bromide-containing waters, though it can also be found in hypochlorite solutions likely from a reaction of bromide with hypochlorite analagous to the formation of chlorate (Asami, Kosaka, and Kunikane 2009). Better refining of salts and/or source water for hypochlorite generation may help remove or reduce the introduction of bromide into the process and final product thereby greatly reducing the amount of bromate formed. It is currently unknown what impacts the presence of bromite and/or bromate will have on the decomposition of hypochlorite and the formation of chlorate and perchlorate in those solutions.

ANALYTICAL METHODS

Prior to 2005, the most commonly applied instrumental analytical technique for measurement of oxyhalide anions was ion-chromatography with conductivity detection (IC-CD). Of those, US EPA methods 300.1 and 314 using IC-CD were the most commonly used methods for the analysis of bromate and perchlorate with reporting limits of 5 µg/L for bromate and 4 µg/L for perchlorate. While IC-CD was successfully applied to many drinking waters, obtaining reliable results in more concentrated samples with higher conductivity was challenging. Furthermore, these methods suffered from potential matrix interferences when applied to environmental mixtures (Urbansky 2000b; Anderson and Wu 2002; Liu, Mou, and Heberling 2002). For example, p-chlorobenzene sulfonate, a compound often found in paints and chemical manufacturing, co-elutes with perchlorate when analyzed by US EPA method 314 (IC-CD method) and interferes with quantitation. (Johnson, Grimshaw, and Richman 2003). Some techniques used to overcome these challenges included pre-concentration steps, such as solid-phase extraction (SPE) and ion-exchange columns, and post-column reactions (derivatizations) followed by UV measurement (IC-PCR) (Inoue, et al. 1997; Bichsel and Von Gunten 1999; Nowack and von Gunten 1999; Salhi and Von Gunten 1999; Magnuson, Urbansky, and Kelty 2000; Urbansky, et al. 2000a; Wagner, et al. 2002; Kirk, et al. 2004). A more sensitive method for bromate analysis was US EPA method 317 using IC-PCR with a reporting limit around 1 µg/L though it was not applicable to other oxyhalides except chlorite. Other approved methods for bromate analysis include US EPA methods 326 and 321.8.

Other non-instrumental approaches to measuring perchlorate and other oxyhalides in aqueous media have included colorimetric determination (Bodenheimer 1955), spectrophotometric determination (Fritz 1964; Prince 1964; Cheng 1967; Weiss 1972), atomic absorption (Collinson 1968), UV absorbance (Soto, et al. 2008), amperometric titration (Clesceri, Greenberg, and Eaton 1998), and direct titration (Adam and Gordon 1995). The direct titration method relies upon the reduction of hypochlorite with sulfite, followed by sequential reduction of chlorite and chlorate ions with iodide, resulting in the stoichiometric production of iodine ions. This allows determination of these ions by iodometry, where the proportional amount of iodine for the reactions with the analyte is titrated with a standardized thiosulfate solution. One advantage of potentiometric methods over IC-CD methods is the selectivity towards specific oxyhalide anions and the ability of the method to be applied to concentrated hypochlorite solutions.

Mass spectrometry is another technique that has been applied for the detection of oxyhalide anions, most commonly in conjunction with ion-chromatography (IC-MS) or liquid chromatography (LC-MS) (Salov, et al. 1992; Urbansky, et al. 1999; Handy, et al. 2000; Koester, Beller, and Halden 2000; Magnuson, Urbansky, and Kelty 2000; Roehl, et al. 2002; Winkler, Minteer, and Willey 2004). The use of mass spectrometry for the detection of ionic compounds increased dramatically with the development of commercially available IC-MS systems (Zwiener and Frimmel 2004). In order to obtain accurate quantitation using IC-MS or LC-MS techniques, many investigators used clean-up techniques to minimize interfering compounds (Urbansky 2000b) or standard addition to compensate for suppression/enhancement artifacts (Batista, McGarvey, and Vieira 2000; Koester, Beller, and Halden 2000; Magnuson, Urbansky, and Kelty 2000). The use of tandem mass spectrometry (MS/MS) and isotope dilution can also be used to add selectivity and accuracy to oxyhalide quantitation methods. US EPA method 331.0 uses LC-MS/MS while US EPA method 332.0 uses IC-MS/MS to detect perchlorate in water, but neither

was developed to identify and quantify other oxyhalides at the same time (USEPA 2005a; USEPA 2005b). A paper by Snyder et al. (2005) demonstrates that LC-MS/MS can be used to measure perchlorate together with bromate, chlorate, and iodate in OSG hypochlorite solutions (Snyder, Vanderford, and Rexing 2005). Furthermore, this paper demonstrates that, under the conditions employed, LC-MS/MS is capable of detecting perchlorate in commercial detergents – which is a significantly more challenging matrix than drinking water. This same method was later adapted to measure perchlorate in aqueous extracts of vitamins and food supplements (Snyder, et al. 2006).

RESEARCH QUESTIONS AND APPROACH

Based on the above considerations, conversations with the Water Research Foundation Project Advisory Committee, and specific objectives from within the AWWA RFP, the Project Team at SNWA identified the following additional research questions designed ultimately to assist the Project Team in determining a mechanism and predictive model for perchlorate formation in hypochlorite solutions:

1. What analytical method(s) is/are the most appropriate for measurement of oxyhalide anions in bulk hypochlorite solutions, OSG solutions, and utility water samples?

2. What hypochlorite quenching agent could be employed for use in sample preservation that would not interfere with the analysis of chlorite, chlorate, perchlorate, bromate, and metals?

3. What effects do the concentration of oxyhalide anions in addition to bromide have on the formation of perchlorate and bromate?

4. What effects do pH, ionic strength, and temperature have on perchlorate formation?

5. Do transition metals catalyze the formation of perchlorate in hypochlorite solutions?

6. Can a detailed chemical rate law be developed to predict (within 30 days of manufacture) perchlorate formation in sodium hypochlorite solutions to within +/- 10% of actual values?

7. What rate law best describes the formation of perchlorate in hypochlorite solutions and what is the reaction order with respect to hypochlorite, chlorate, and any other contributing anions?

8. Is a simple mechanism available to describe the formation of perchlorate from hypochlorite and chlorate?

Additional questions were also asked regarding operational considerations, hypochlorite sources, on-site generation, and other factors for DWTPs:

9. Is there a significant difference in the perchlorate concentration measured in fresh bulk hypochlorite and different OSG systems including those operated in mixed oxidant mode?

10. To what extend could the use of OSG or bulk hypochlorite adversely affect perchlorate concentration in finished drinking water considering the NSF 60 maximum use level (MUL) of 10 mg/L (NSF/ANSI 2005)?

11. What recommendations can be made to drinking water utilities to minimize the presence of perchlorate, bromate, chlorate, and chlorite in hypochlorite solutions used for drinking water treatment?

Research Approach

In order to answer the questions outlined above the Project Team designed a four-tiered approach to completing the project within the allowed 11-month period. The overarching objective of this study was to evaluate the magnitude of perchlorate contamination in chemically and electrochemically manufactured hypochlorite solutions, to determine the impact on finished drinking water contamination, to provide utilities with a way to predict perchlorate concentration in hypochlorite solutions, and to devise techniques to minimize the formation of perchlorate in hypochlorite solutions. The specific task outlined in the Project Proposal included the following:

Task 1: Comprehensive Literature Review
Task 2: Analysis of Impurities in Hypochlorite
Subtask 2.1: Perchlorate in Commercially Available Hypochlorite
Subtask 2.2: Impact of transition metals on perchlorate formation
Subtask 2.3: Determination of Factors Related to Perchlorate Formation and Minimization in Hypochlorite
Task 3: Treatment/Manufacturing System Impact on Drinking Water
Task 4: Recommendations and Final Report

Task 1: Literature Review

The initial phase of this study involved a review of available literature regarding hypochlorite and perchlorate chemistry, analytical methodologies, and current occurrence data. A significant portion of the literature review for this study was completed prior to the Project Kickoff (May 9, 2008) and was used to identify experiments necessary in the early stages of the project. The literature review was an ongoing process during the course of the Project whereby additional papers found in the literature were used to further refine the experimental matrix and guide the completion of this Final Report.

Task 2: Impurities Analysis

This Project Team had previously developed robust analytical methodologies that were able to identify and quantify accurately and precisely perchlorate in hypochlorite solutions at sub-µg/L concentrations (Snyder, Vanderford, and Rexing 2005). The methodology utilized LC-MS/MS technology with an isotopically labeled (^{18}oxygen) perchlorate as an internal standard.

The methods developed by SNWA researchers allowed for the simultaneous, direct LC-MS/MS measurement of perchlorate, chlorate, and bromate in hypochlorite solutions and drinking water samples. However, for the purposes of understanding the factors which impact the formation of perchlorate, the decision was made to devote several weeks at the beginning of the project towards determining whether the LC-MS/MS method or the titrimetric method would provide more accurate and precise quantitation. Once the method of choice was clearly identified for use in concentrated hypochlorite solutions, then the Project Team could focus on the mechanistic studies.

Subtask 2.1: Perchlorate in Commercially Available Hypochlorite Prior to collecting, shipping, and analyzing any hypochlorite samples, the effect that preservatives / quenching agents had on the presence, formation, or decay of any species of consideration (oxyhalides, chloride, bromide, and metals) had to be quantified. The commonly used quenching agent used to treat residual hypochlorite prior to mass spectrometric measurement of perchlorate ion had been hydrogen peroxide (Urbansky 2000c). However, it was not clear that the use of peroxide would be the best quenching agent for this study. Thus, a total of seven quenching agents (hydrogen peroxide, ascorbic acid, glycine, malonic acid, oxalic acid, sodium thiosulfate, and sodium sulfite) were tested for the removal (quenching) of hypochlorite and the impact on other contaminants of concern. The criteria for the best quenching agent included ease of handling, safety, rate of reaction with hypochlorite, absence of adventitious impurities in the quenching agent, and stability.

After selection of a quenching agent and analytical method, a series of commercially available hypochlorite solutions and OSG solutions were tested for perchlorate, bromate, bromide, and transition metals. Additionally, seven utilities were asked to provide hypochlorite and treated water samples for oxyhalide and metals analysis. A commercially available 13% sodium hypochlorite solution was chosen as the baseline for kinetics studies and was aged at different dilutions with varying concentrations of chlorate, chlorite, chloride, bromide, bromate, ionic strength, pH, and transition metals. Temperatures were varied for batch studies from 30 °C to 75 °C. In total, over 3,800 individual data points were collected for elucidation of the mechanism described in this Report. Similarly, over 1,500 individual data points were collected from the OSG and Utility hypochlorite samples, aged at 50 °C, and used to validate the model predictions. The study also included over 120 individual data points for the surveyed raw, finished, and distribution waters.

Subtask 2.2: Impact of transition metals on perchlorate formation In previous studies of the decomposition of hypochlorite to form chlorate, transition metal ions have been shown to have very important catalytic properties (Gordon, et al. 1993; Gordon, Adam, and Bubnis 1994; Gordon, Adam, and Bubnis 1995). Nickel ion, for example at the 1 – 2 mg/L level, was shown to enhance the rate of hypochlorite decomposition by more than a factor of ten. Other transition metal ions such as cobalt(II) and copper(II) may also impact the rate of hypochlorite loss though manganese(II) iron(II) seem to have little to no effect. These transitions metal ions represent those that are most likely to be present in commercial hypochlorite and potentially impact perchlorate formation. Thus, a series of experiments were also carried out as part of the concentration matrix (from Subtask 2.1) at 0.2, 2, and 20 mg/L of nickel(II), manganese(II), iron(II), cobalt(II), and copper(II). In addition, noble metals ions (Ag, Au, Ir, Pd, Pt) at 0.2 mg/L were also included as part of this task.

Subtask 2.3: Determination of Factors Related to Perchlorate Formation and Minimization in Hypochlorite This task was designed determine the factors in hypochlorite manufacturing and handling that would have the greatest impact on the formation of perchlorate in hypochlorite solutions. The Project Team used experiments from this task to assist in developing clear strategies for minimizing the formation of perchlorate in both hypochlorite manufacturing and on subsequent storage/handling. Temperature, hypochlorite concentration, and presence of metal ions were all investigated as each plays an important role in hypochlorite degradation (Gordon, Adam, and Bubnis 1994). Experiments under this task included aging hypochlorite solutions at various temperatures, pH, bromide, and metal ion concentrations, and collecting samples for perchlorate and bromate analysis as a function of time. The loss of hypochlorite and the formation of perchlorate were monitored during this portion of the study.

Task 3: Systems Impact (Influence of Hypochlorite in Perchlorate Contamination of Drinking Water)

This task was designed to provide a means for determining the degree of perchlorate contamination in finished drinking water attributable to hypochlorite. Specific experiments were designed to create a detailed chemical rate law ("Predictive Model") in order to understand the kinetic processes influencing the rate of perchlorate build-up in freshly prepared and aging hypochlorite solutions as a function of hypochlorite, chlorate, and chloride concentrations, pH, storage temperature, ionic strength, and metal ion concentration. The results of these experiments were used to develop a preliminary mathematical model from the detailed chemical rate law describing the role of each of the experimental variables in the formation of perchlorate along with the appropriate uncertainties (similar to the Adam and Gordon chlorate ion "Bleach 2001" model). The objective was to develop a "Predictive Model" that would take into account the sources of perchlorate (*e.g.*, the sodium hydroxide, the manufacturing of hypochlorite, and the continued decomposition of hypochlorite) as a function of hypochlorite, chlorate, chloride, and storage temperature and be used to assist in making specific, quantitative recommendations to utilities to minimize perchlorate formation. Additionally, several calculations were used to determine minimum, median, and maximum concentrations of perchlorate that could be expected at a typical water treatment facility based upon hypochlorite age, storage conditions (temperature and dilution), and dose.

In this phase of the project, several commercially available on-site hypochlorite generators and feed systems were also evaluated. The Project Team collected and analyzed brine streams prior to electrolytic conversion for perchlorate, chloride, metals, and other water quality constituents that may impact hypochlorite degradation and perchlorate formation. Additionally, water from the participating utilities (that also supplied hypochlorite solutions for perchlorate analysis) was used to conduct simulated distribution system (SDS) tests to determine if perchlorate would be formed in the distribution system. Actual samples from the distribution systems of participating utilities were also analyzed for perchlorate. Distribution system samples included locations having maximum chlorine contact time.

Task 4: Recommendations and Final Report

The conclusions from this research study will hopefully provide the water industry with the information needed to minimize perchlorate formation in hypochlorite solutions. Dissemination of the findings from this study include presentations and industry conferences, publication in peer-reviewed journals, and this Final Report. A complete list of recommendations for utilities using bulk hypochlorite or OSG hypochlorite can be found in the Executive Summary and in Chapter 6.

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CHAPTER 2
ANALYTICAL METHODS

BACKGROUND

One of the most crucial components underlying the successful completion of this project was the validation of analytical methods for applicability in the broad array of matrices under investigation. Method validation was necessary to ensure that any empirical observations made during the course of the project could be related to precise and accurate concentrations of contaminants (within +/- 5%) in any given matrix, from 13% hypochlorite to 1% on-site generated (OSG) hypochlorite to distribution system samples with 1 ppm chlorine residual or less. Multiple analytes were identified in the initial stages of this study that had potential roles in the formation of perchlorate including transition metals (e.g., Mn, Fe, Co, Ni, and Cu), hypochlorite, chlorite, chlorate, perchlorate, bromide, and bromate. While the role of individual analytes in perchlorate (and bromate) formation could be hypothesized, good quantitation was key to the successful determination of a detailed chemical rate law. Some of the challenges in analyzing for each of the contaminants of concern included:

- Working with concentration ranges from g/L levels in concentrated hypochlorite solutions to low μg/L levels in distribution system samples, resulting in massive dilution factors (and associated error) in some cases
- High levels of hypochlorite and other salts which could potentially damage the analytical instruments
- High levels of chloride in the hypochlorite solution which can overload the liquid chromatography (LC) column and mask the presence of other analytes
- Detection of low levels of transition metals in hypochlorite solutions and distribution system samples
- Selection of a quenching agent for hypochlorite that would not contaminate or interfere with the analysis of any of the analytes of concern in the various samples collected at the SNWA laboratory or hundreds of miles away at each of the participating utility sites.

Given each of the concerns listed above, the approach for method development involved multiple steps, several of which were performed simultaneously. For the purpose of this report, however, the method development and application are listed in the most logical order for interpretation of data within the report and for future use: sample handling techniques, an overview of LC-tandem mass spectrometry (LC-MS/MS) and titrimetric methods, comparison of the methods (titration methods for use in concentrated hypochlorite solutions and LC-MS/MS for OSG and water samples), selection of a quenching agent, and metal ion quantification in hypochlorite solutions and water. For ease of use, a flow-chart summarizing the method decision making process is shown in Figure 2.1.

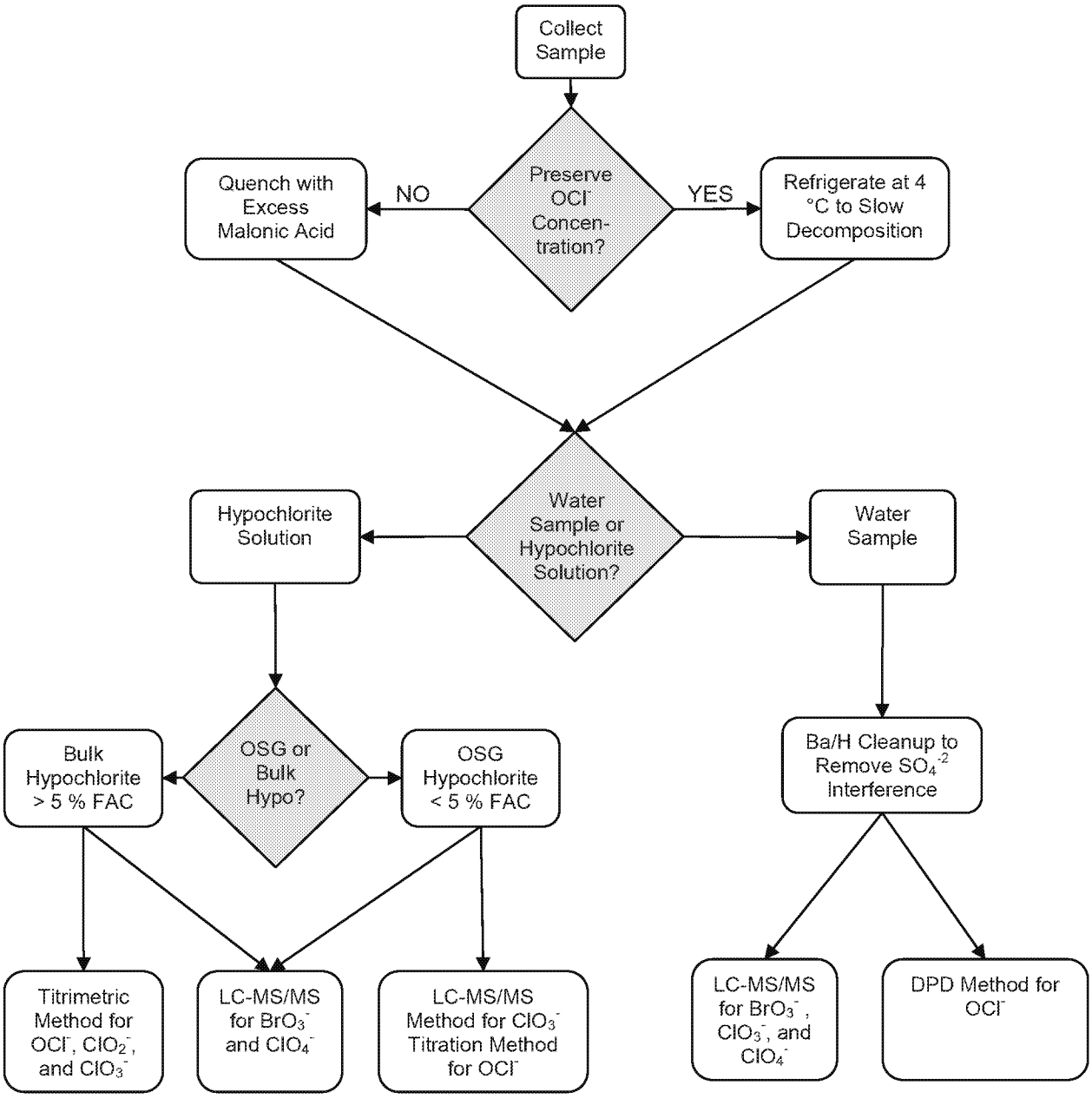

Figure 2.1 Decision tree for sample processing and analysis depending upon the type of information required and the type of sample being collected

ANALYTICAL METHODS

Sample Collection and Handling

Sodium Hypochlorite Samples

As sodium hypochlorite solutions decompose over time, thereby producing more perchlorate, controlled storage of the samples was preferred. Thus, two choices were available for this study: either quench the hypochlorite to stop subsequent formation and/or decomposition reactions or cool the samples to 4 °C to slow reaction rates significantly below those observed at room temperature. Quenching ensures the most accurate measurements of perchlorate, chlorate, and bromate when a time-of-sampling measurement is desired. Storing samples at 4 °C preserves hypochlorite (which is important for rate determination and modeling) and decreases the loss of hypochlorite significantly, thereby allowing the sample to be analyzed for hypochlorite in addition to chlorate, perchlorate, and bromate. Furthermore, unquenched samples can be used for holding studies to examine rates of formation of contaminants. For this study, duplicate samples were collected in acid-washed high-density polyethylene (HDPE) bottles and split: one sample was preserved with malonic acid while the other was cooled to 4 °C and prepared for shipment on ice to the SNWA laboratory. The reaction between hypochlorite and malonic acid is mild and slow (many minutes) and no special handling was required. However, one hour of reaction time was allowed to ensure complete quenching of hypochlorite. Malonic acid was used to quench hypochlorite in a 0.75:1 mol ratio, or approximately 11 g malonic acid for every 10 g FAC expected.

Water Samples

Water samples were collected using 125 mL, acid-washed HDPE bottles that were pre-dosed with 13 µL of a 1 M malonic acid stock solution for quenching up to 10 mg/L residual hypochlorite. Sample bottles were filled, capped, and stored at 4 °C to minimize evaporation. The perchlorate anion is very stable and does not precipitate easily, thus no pH adjustments were necessary. Once collected, the water samples were sequentially passed through one OnGuard II Ba and one OnGuard II H Cartridge (Dionex, Sunnyvale, CA) to reduce sulfate and carbonate ion concentrations. These anions have been previously shown to suppress oxyhalide concentrations when using LC-MS/MS for analysis (Snyder, Vanderford, and Rexing 2005). Care was also taken to assess the necessary cartridge capacity, as water samples have varying sulfate and carbonate ion concentrations depending on their geological background. Samples also were filtered using 0.2 µm surfactant free cellulose acetate filters (Fisher Scientific, Pittsburg, PA) to remove any suspended particulates.

LC-MS/MS Method for Bromate, Chlorate, and Perchlorate Analysis

EPA 314.0, which relies on ion chromatography (IC) coupled with conductivity detection, has long been used for the analysis of perchlorate in water. Conductivity detection is inherently a non-selective technique, as many components in aqueous mixtures are conductive, and, as a result, this method has been shown to produce false positives, where perchlorate is incorrectly identified (Johnson, Grimshaw, and Richman 2003; Mathew, Gandhi, and Hedrick 2005). This has led to the development of mass spectrometric methods for the detection and quantification of perchlorate and other oxyhalides in water (Handy, et al. 2000; Koester, Beller,

and Halden 2000; Magnuson, Urbansky, and Kelty 2000; Magnuson, Urbansky, and Kelty 2000; Richardson 2002; Roehl, et al. 2002; Rickman 2003; Gandhi, Johnson, and Joe 2004; Winkler, Minteer, and Willey 2004; Zwiener and Frimmel 2004; Snyder, Vanderford, and Rexing 2005), as these methods have been shown to be much more selective and sensitive than IC-conductivity detection. In addition, the EPA has recently released two methods for the measurement of perchlorate in water, EPA 331 and 332, using LC-MS and IC-MS, respectively (USEPA 2005a; USEPA 2005b). However, due to the unique challenges being posed by the matrices of interest, this project required a method that has been proven to be reliable in very complex matrices.

In 2005, an LC-MS/MS method developed by Snyder, et al., was published that demonstrated the reliable analysis of perchlorate in water (Snyder, Vanderford, and Rexing 2005). This method was also shown to be capable of detecting perchlorate in challenging matrices such as commercial detergents and was later adapted to measure perchlorate in aqueous extracts of vitamins and food supplements (Snyder, et al. 2006). In addition, it allowed the simultaneous identification and quantification of bromate and chlorate. Therefore, it was selected as the basis for the method used in this project to measure low level concentrations of oxyhalide anions in water and OSG samples.

Although the method discussed above was based on the work by Snyder, et al., some modifications were made. Analytes were separated using a 75 x 4.6 mm Synergi Max-RP C12 column with a 4 µm pore size (Phenomenex, Torrance, CA). A binary gradient consisting of 0.1% formic acid (v/v) in water (A) and 100% methanol (B) at a flow rate of 700 µl/min was used. The gradient was as follows: 2% B held for one minute, increased linearly to 15% B by two minutes, changed to 95% B and held for four minutes, and finally changed to 2% B and held for 3 minutes. A one minute equilibration step at 2% B was used at the beginning of each run to bring the total run time per sample to 10 minutes. An injection volume of 20 µl was used for all samples.

Tandem mass spectrometry was performed using a triple-quadrupole mass spectrometer equipped with an electrospray ionization source operated in negative ion mode (Applied Biosystems, Foster City, CA). In tandem mass spectrometry, a target analyte is first ionized in the ionization source and selected for the first quadrupole. Subsequently, the precursor ion is fragmented in the second quadrupole and a representative fragment (product ion) of the precursor is selected for in the third quadrupole. The monitoring of this transition from precursor to product ion makes the mass spectrometer very selective and sensitive. For this method, the following precursor/product ion transitions were used: $^{35}ClO_4^-$ (*m/z* 99) to $^{35}ClO_3^-$(*m/z* 83) for perchlorate; $^{35}ClO_3^-$ (*m/z* 83) to $^{35}ClO_2^-$ (*m/z* 67) for chlorate; and $^{79}BrO_3^-$ (*m/z* 127) to $^{79}BrO_2^-$ (*m/z* 111) for bromate.

To ensure the proper identification of the oxyhalides, additional ion transitions of perchlorate, chlorate and bromate using naturally occurring, stable isotopes of chlorine and bromine (chlorine-37 and bromine-81) were simultaneously monitored for purposes of confirmation. The following confirmation transitions were used: $^{37}ClO_4^-$ (*m/z* 101) to $^{37}ClO_3^-$ (*m/z* 85) for perchlorate; $^{37}ClO_3^-$ (*m/z* 85) to $^{37}ClO_2^-$ (*m/z* 69) for chlorate; and $^{81}BrO_3^-$ (*m/z* 129) to $^{81}BrO_2^-$ (*m/z* 113) for bromate.

In addition, perchlorate and bromate were quantified using the isotope dilution technique. In isotope dilution, a non-radioactively labeled analog of each target compound is added to every sample and the recovery of the labeled compound is used to determine the degree of matrix interference in the sample for each target analyte (Vanderford and Snyder 2006). Because the labeled compound behaves very similarly to the unlabeled target compound, the recovery can

then be used to correct for matrix interferences. For this project, labeled versions of perchlorate ($^{35}Cl^{18}O_4$) and bromate ($^{79}Br^{18}O_4$) were used that contain oxygen-18, a stable isotope of oxygen that occurs at only 0.20% in nature. As no source of oxygen-18 labeled chlorate was commercially available, it was quantified using external calibration.

Based on published results and other preliminary tests in our laboratory, the method reporting limits (MRL) for each matrix were determined and are shown in Table 2.1. (Note: The concentrated hypochlorite solution detection limits are based on a standard dilution factor of 1:100, though MRLs may be adjusted upwards for increased sample dilution.)

Table 2.1
LC-MS/MS MRLs (µg/L) for target analytes in water and hypochlorite solution

	Water	Hypochlorite solution
Perchlorate	0.05	5.0
Bromate	0.1	10
Chlorate	0.1	10

Titration Method for Hypochlorite, Chlorite, and Chlorate Analysis

While the LC-MS/MS method was validated and shown to be appropriate for use in water samples and in dilute hypochlorite solutions (i.e., OSG hypochlorite), a titrimetric technique was employed to measure oxychloride anions in bulk hypochlorite solutions. The titration technique used for this study was based in part on an older iodometric technique for chlorate determination (Equations 2.1, 2.2, and 2.3). This technique relies upon the fact that hypochlorite, chlorite, and chlorate ions react with iodide ion to produce iodine. This allows determination of chlorate but the technique is unable to differentiate chlorite and hypochlorite. The determination is based upon a proportional amount of iodine reacting with the analyte (shown below) followed by addition of excess concentrated hydrochloric acid to affect a color change, after which chlorate can then be titrated.

$$OCl^- + 3I^- + 2H^+ \rightarrow I_3^- + Cl^- + H_2O \quad \text{pH 1.3} \quad \textbf{(2.1)}$$

$$ClO_2^- + 6I^- + 4H^+ \rightarrow 2I_3^- + Cl^- + 2H_2O \quad \text{pH 1.3} \quad \textbf{(2.2)}$$

$$ClO_3^- + 9I^- + 6H^+ \rightarrow 3I_3^- + Cl^- + 6H_2O \quad \text{6M } H^+ \quad \textbf{(2.3)}$$

A well established way to make a standard solution of triiodide is to add a known amount of iodate to an acidic solution containing a small excess of iodide:

$$IO_3^- + 8I^- + 6H^+ \leftrightarrow 3I_3^- + 3H_2O \quad \textbf{(2.4)}$$

The prepared standard solution of I_3^- can then be used to standardize thiosulfate and sulfite solutions:

$$I_3^- + 2S_2O_3^{2-} \rightarrow 3I^- + S_4O_6^{2-} \quad \textbf{(2.5)}$$

$$I_3^- + SO_3^{2-} + 2OH^- \rightarrow SO_4^{2-} + 3I^- + H_2O \quad \textbf{(2.6)}$$

Many variations of iodometric titration methods have been developed over the years. However, potentiometric titration of hypochlorite with sulfite allows selective determination of hypochlorite ion from chlorite ion (Gordon, et al. 1993; Adam 1994). This potentiometric titration technique was used and validated in previous work to study the decomposition of hypochlorite and the subsequent formation of chlorite and chlorate in concentrated hypochlorite solutions (Gordon, et al. 1993; Adam 1994; Adam and Gordon 1995; Gordon, et al. 1997). Given the previous validation and expertise within the Project Team, the potentiometric method was used for analysis of oxychloride anions in concentrated hypochlorite solutions. The sequential determinations of specific anions were carried out in five sequential steps as outlined in Equations 2.7 – 2.11:

Step 1: Titration of OCl^- at pH 10.5:

$$OCl^- + SO_3^{2-} \rightarrow SO_4^{2-} + Cl^- \quad \textbf{(2.7)}$$

Step 2: Removal of excess SO_3^{2-} at pH 10.0 – 10.5:

$$I_3^- + SO_3^{2-} + 2OH^- \rightarrow SO_4^{2-} + 3I^- + H_2O \quad \textbf{(2.8)}$$

Step 3: Removal of excess I_3^- at pH 9 – 10.5:

$$I_3^- + 2S_2O_3^{2-} \rightarrow 3I^- + S_4O_6^{2-} \quad \textbf{(2.9)}$$

Step 4: Determination of ClO^{2-} at pH 1.3:

$$ClO_2^- + 6I^- + 4H^+ \rightarrow 2I_3^- + Cl^- + 2H_2O \quad \textbf{(2.10)}$$

Step 5: Determination of ClO_3^- after addition of concentrated HCl :

$$ClO_3^- + 9I^- + 6H^+ \rightarrow 3I_3^- + Cl^- + 3H_2O \qquad 6M\ H^+ \quad \textbf{(2.11)}$$

Titrations with sulfite were carried out using a VIT 90 Video Titrator with a P101 platinum k401 SCE electrode pair (Radiometer, Copenhagen, Denmark). Titrations with thiosulfate were performed with a standard 50 mL laboratory glass burette. Concentrated hydrochloric acid (ACS reagent grade, Fisher Scientific, Pittsburg, PA) and the sample solution were purged with nitrogen gas to minimize oxidation of iodide by oxygen prior to chlorate determination. Potassium iodate standard (0.1 M) was prepared weekly using high purity (>99.4%) potassium iodate and used to standardize sulfite and thiosulfate solutions daily. Standardization by this method resulted in standard deviations of less than three parts per thousand and less than 1% relative standard deviation. The 0.2 M SO_3^{2-} solutions were prepared from ACS reagent grade sodium sulfite. The 0.1 M $S_2O_3^{2-}$ solutions were prepared from ACS reagent grade sodium thiosulfate.

ICP-MS Method for Metals Analysis in Sodium Hypochlorite Solutions

Metal ion analysis and quantification was carried out using US EPA method 200.8 on an Agilent (Palo Alto, CA) 7500c Inductively Coupled Plasma-Mass Spectrometer (ICP-MS) with an Octopole Reaction System that uses hydrogen-helium reaction gas to remove Ar-based isobaric and polyatomic oxide interferences. Internal standards were used to correct for matrix interferences. Dilutions ranging from 1:10 to 1:500 were used to reduce the impact of the high total dissolved solids (TDS) background of hypochlorite samples. Actual MRLs are summarized in Table 2.2.

Table 2.2
ICP-MS method reporting limits (µg/L) in water and hypochlorite solutions

Metal	Water*	Hypochlorite solution*
Manganese (Mn)	1.0	25
Iron (Fe)	5.0	125
Cobolt (Co)	2.0	25
Copper (Cu)	5.0	25
Nickel (Ni)	1.0	25

*Occasionally higher MRLs are shown in the text when higher dilution factors were used; the MRLs listed are the lowest level at which data are reported in the text of this report; The proportionality of MRLs between water and hypochlorite varied based on required dilution factors

Specific Conductance, Ionic Strength, and pH Measurements

Specific conductance measurements were performed using a HACH Ion-Series Conductivity/Total Dissolved Solids meter (Hach Company, Loveland, CO). A calibration was performed using a 1,000 µmho/cm standard prior to sample analysis. In most cases dilutions were required to bring the conductivity to within the linear range of the probe. Specific conductance was measured in order to determine the ionic strength of hypochlorite solutions. Ionic strength (I) was calculated from specific conductance (σ) using Equation 2.12:

$$I\ (mol/L) = 1.6 \times 10^{-5} \times \sigma\ (\mu mho/cm) \qquad \textbf{(2.12)}$$

Total dissolved solids (TDS) could also be approximated by Equation 2.13:

$$TDS\ (mg/L) \sim I * 4 \times 10^{4} \qquad \textbf{(2.13)}$$

An AP62 pH/mV Meter (Fisher Scientific, Pittsburg, PA) was used to measure sample pH. Meter calibrations using standard pH buffers (pH 4, 7, 10) was performed prior to measurements of samples.

Quality Assurance and Quality Control

Quality assurance and quality control followed EPA Method 331 for LC-MS/MS analysis and EPA Method 200.8 for metals analysis. Significant time was devoted to validate the use of the quenching agent of choice (malonic acid) and to validate the methods for applicability to each matrix (e.g., LC-MS/MS for OSG and water, titrations for bulk hypochlorite). Validation was performed using matrix spikes, blanks, and split samples for comparison.

METHOD VALIDATION

Selection of Quenching Agent

The selection of a hypochlorite quenching agent was critical for the monitoring component of this project and for experiments that were conducted off-site at a manufacturing facility. Some initial concern was raised about the potential negative impact of unquenched hypochlorite ions on the mass spectrometer, though this turned out not to be a factor and thus was not a major component in the decision making process. For any experiments performed on-site where chemical reactions/reaction rates needed to be stopped or attenuated, simply refrigerating the sample aliquots at 4 °C significantly slowed the reaction: the half life of 13% NaOCl solution at 25 °C is 130 days, at 4 °C the half life is 3184 days, according to the Bleach 2001 Predictive Model (Adam, Gordon, and Pierce 2001). Thus, temporary storage of concentrated hypochlorite samples at 4 °C (for up to several weeks) still allowed accurate determinations of hypochlorite and perchlorate concentrations. However, in cases where precise temperature control was not possible or was in question, the use of a quenching agent was necessary for the quantification of other ionic species present in the hypochlorite solutions or water sample.

A total of seven hypochlorite quenching agents were investigated for use in this project based on descriptions in the literature (Gordon 1990; Wood 1990; Sweetin 1993; Adam 1995; Liu 2003) and from current practices at the SNWA laboratory. The quenching agents tested included ascorbic acid, malonic acid, oxalic acid, glycine, sodium sulfite, sodium thiosulfate, and hydrogen peroxide. The selection of the final quenching agent was based on the following criteria:

- Safety, ease of handling, transport, and stability
- Ability to quench hypochlorite reproducibly
- No appreciable impact on bromate levels
- No appreciable impact on chlorate levels
- No appreciable impact on perchlorate levels
- Amount of transition metals present in appreciable concentration to impact analysis (i.e., contamination)
- Number of moles required and cost
- Compatibility with iodometric determination (i.e., quenching agent does not react with iodide or interfere with titration method)

Safety, Ease of Handling, Transport, and Stability

Several of the quenching agents under consideration (hydrogen peroxide, glycine, and oxalic acid) reacted vigorously with hypochlorite, causing significant loss of sample during the reaction, and/or produced heat and noxious fumes. Concentrated solutions of hydrogen peroxide (32% w/w) require special handling and quenching 10 mL of 13% sodium hypochlorite solution produced a considerable amount of heat and gas, making this quenching agent the most dangerous to use. Glycine, though relatively safe itself, reacted violently and produced a very noxious gas when reacted with hypochlorite that can potentially cause light-headedness, dizziness, and nausea. The remaining quenching agents also produced heat and gas, but to a lesser extent. Ascorbic acid reacted the least vigorously and appears to be the safest quenching agent tested. None of the quenching agents had associated transportation restrictions (other than including MSDS information with each shipping carton) with the exception of concentrated hydrogen peroxide.

Regarding stability, hydrogen peroxide and sodium sulfite in solution have limited stability and limited shelf-lives. In solution, sodium sulfite may decay by as much as 1% per hour (Adam and Gordon 1995) but may be more stable if used as a solid salt. Ascorbic acid produced marked color changes that can interfere with titrimetric analyses, both during storage of a 1 M stock solution (Figure 2.2) and after quenching of utility hypochlorite samples. Stock solution color change ranged from a colorless solution upon first preparation, to a yellow solution after 20 days of storage at 4 °C, to a dark red solution after 37 days of storage at 4 °C. Quenched hypochlorite solutions exhibited similar color changes due to presence of excess ascorbic acid (Figure 2.3). The development of color in quenched concentrated hypochlorite samples would interfere with the determination of chlorate ion concentration because the iodometric titration has a colorless end-point.

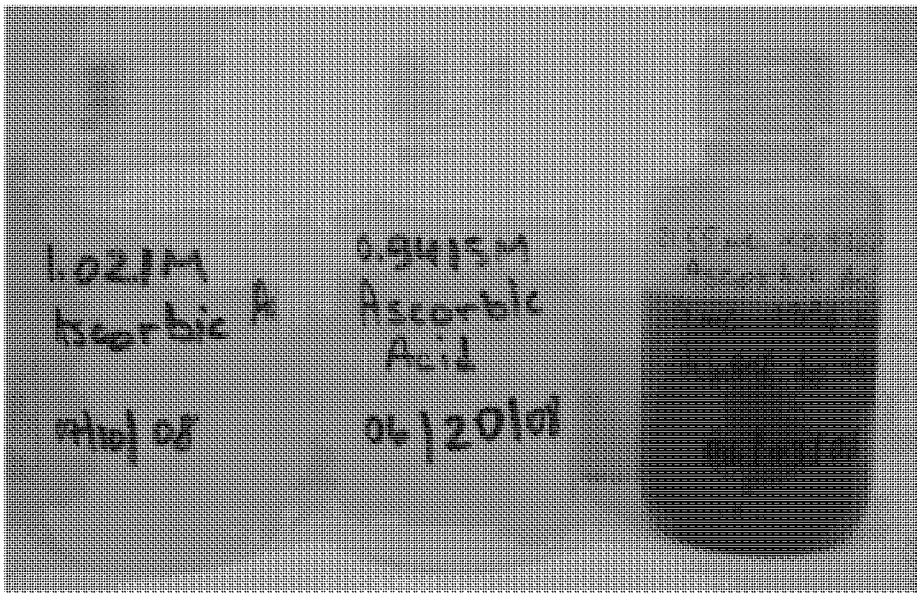

Figure 2.2 Stock solutions of ascorbic acid at t = zero (left), t = 20 days old (center), and t = 37 days old (right)

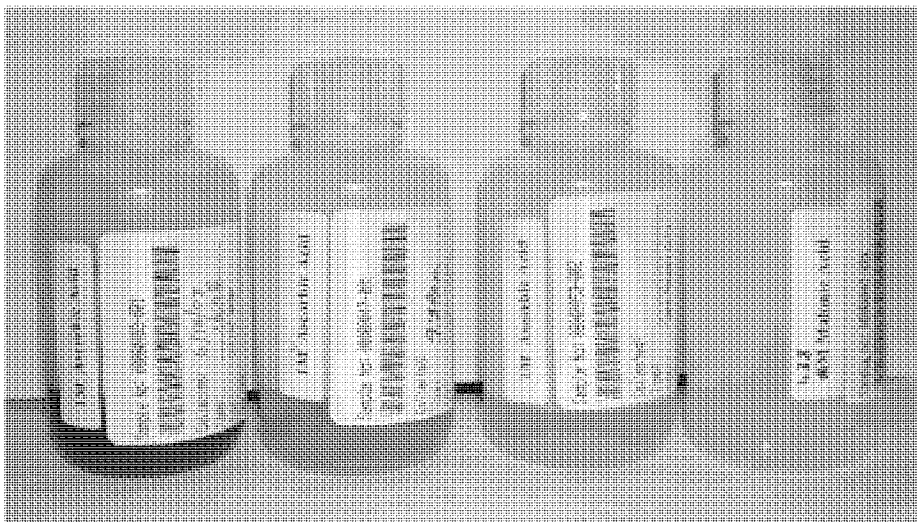

Figure 2.3 Quenched hypochlorite samples from utilities using ascorbic acid (left 3 bottles) and malonic acid (right bottle)

Ability to Quench Hypochlorite Reproducibly

All quenching agents tested were able to quench hypochlorite in test samples. Ascorbic acid, malonic acid, and oxalic acid were able to quench hypochlorite in different concentration and volume solutions of hypochlorite. The mole ratio of quenching agent to hypochlorite (OCl^-) was 1.2 for ascorbic acid, 0.75 for malonic acid, and 1.5 for oxalic acid. Glycine was the least reproducible quenching agent with mole ratios varying from 0.20 to 0.53; one hypothesis is that the reaction is temperature, pH, and mixing dependent and thus may produce variable results depending on sample composition and handling. Oxalic and malonic acids were the slowest reactants, requiring up to one hour for complete quenching of 13% hypochlorite solution. Sodium thiosulfate and sodium sulfite were found to quench hypochlorite reproducibly, though the sodium sulfite had to be standardized prior to use in order to determine the volume required to deliver the appropriate moles of quenching agent.

Impact on Bromate, Chlorate, and Perchlorate Measurements

In early experiments, sodium thiosulfate and sodium sulfite were observed to have an effect on the analysis of bromate by LC-MS/MS. Both bromate and the internal standard were negatively impacted by the presence of thiosulfate and sulfite. Chromatograms of the non-quenched, sulfite-quenched, and thiosulfate-quenched, 13% sodium hypochlorite samples are shown in Figures 2.4 – 2.6. The chromatograms of a non-quenched sample (Figure 2.4) versus sulfite- (Figure 2.5) and thiosulfate- (Figure 2.6) quenched samples illustrate the observed effects on LC-MS/MS analysis of bromate. In Figure 2.4, the internal standard peak height is around 300 counts (retention time 2.04 min) and effectively corrects for matrix effects, with observed average recoveries in spiked samples (n=3) at 91%. For samples quenched using sulfite and thiosulfate, peak shifts, peak attenuation (Figures 2.5, 2.6), and peak splitting (Figure 2.5) were observed. Furthermore, severe matrix suppression of both analyte and internal standard signals hindered the ability for adequate correction, yielding poor recoveries for samples quenched with thiosulfate (60%, n = 3) and no quantifiable recoveries for samples quenched with sulfite. Ascorbic acid also negatively impacted analysis of bromate. When hypochlorite solutions, quenched with ascorbic acid were analyzed, no detectible concentration of bromate was observed. Furthermore, spiked ascorbic acid-quenched hypochlorite solutions with bromate standard, showed much lower recoveries (49%, n=3) than the non-quenched hypochlorite solutions, indicating that excess ascorbic acid in fact may reduce bromate concentration (shown in Table 2.3). The observation of sulfite, thiosulfate, and ascorbic acid reduction of bromate is similar to that made by Keith *et al.* (2006) where sulfite was similarly shown to reduce bromate in gastric juices. The remaining quenching agent (malonic acid) was shown to have no impact on bromate analysis. Recovery data obtained by LC-MS/MS analysis of dilute hypochlorite samples for the remaining quenching agents are shown in Table 2.3.

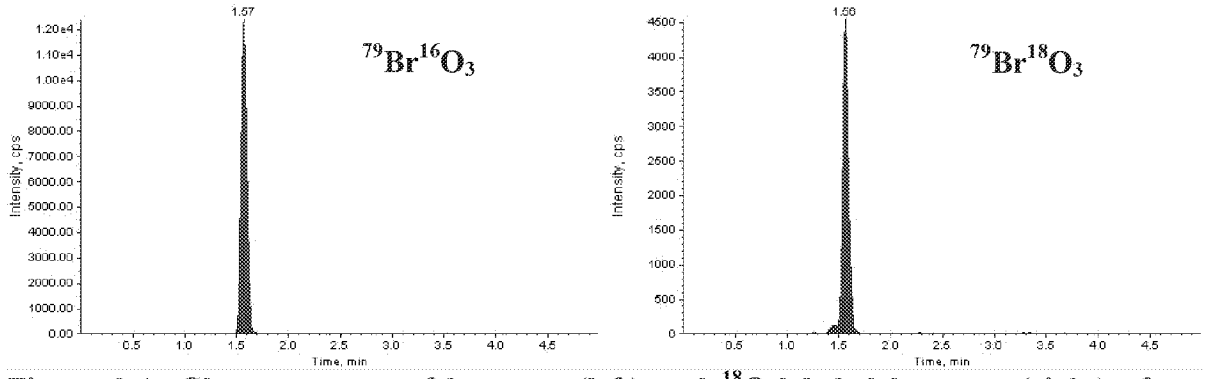

Figure 2.4 Chromatogram of bromate (left) and ^{18}O-labeled bromate (right) of a non-quenched sample of 13% sodium hypochlorite solution diluted by a factor of 1:10,000

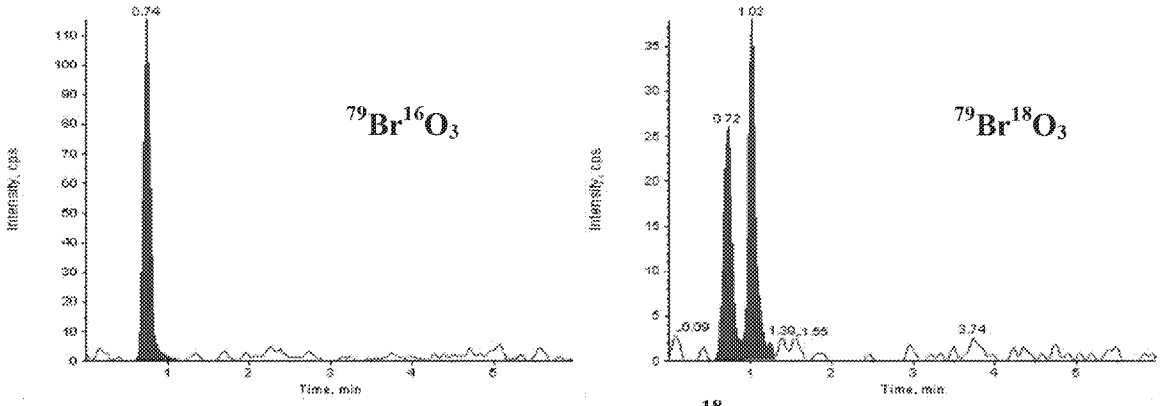

Figure 2.5 Chromatogram of bromate (left) and ^{18}O-labeled bromate (right) of a sulfite-quenched sample of 13% sodium hypochlorite solution diluted by a factor of 1:10,000

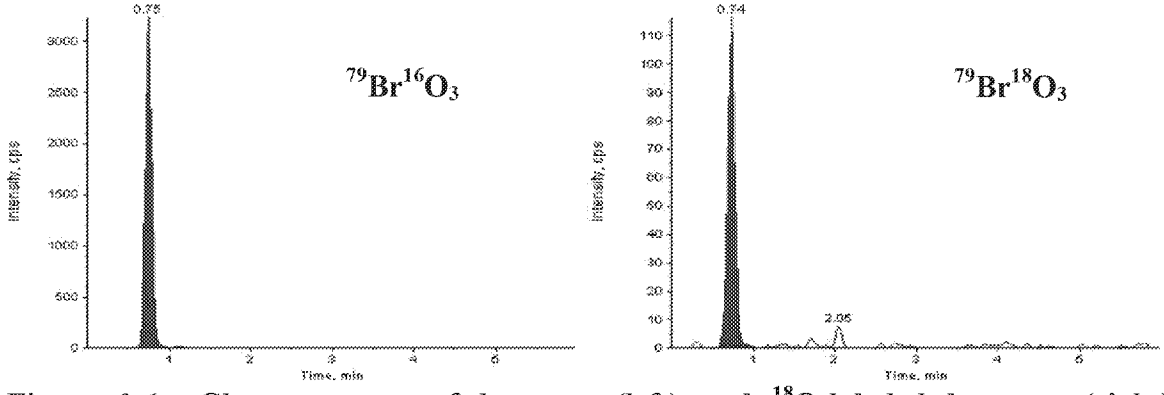

Figure 2.6 Chromatogram of bromate (left) and ^{18}O-labeled bromate (right) of a thiosulfate-quenched sample of 13% sodium hypochlorite solution diluted by a factor of 1:10,000

Table 2.3
Effects of quenching agent on analysis of chlorate, perchlorate, and bromate (n=3)

LC-MS/MS results	Non-quenched hypochlorite	Ascorbic acid	Malonic acid
Chlorate, g/L	16.1 ± 0.15	14.1 ± 0.25	15.7 ± 0.15
Chlorate recovery (matrix spike)	90.8 ± 4	96.2 ± 3	88.9 ± 0.5
Perchlorate mg/L	7.41 ± 0.10	7.42 ± 0.9	7.12 ± 0.5
Perchlorate recovery (matrix spike)	101 ± 1.8	107+1.7	104 ± 2.3
Bromate, mg/L	16.01 ± 0.25	Non-Detect	14.80 ± 0.09
Bromate recovery (matrix spike)	94.3 ± 6.5	*48.6 ± 2.2	96.7 ± 1.1

*Value based on bromate spike in non-quenched hypochlorite sample.
This indicates excess ascorbic acid may reduce bromate concentration.

Number of Moles Required and Cost

Several quenching experiments were performed in order to determine the stoichiometric amounts of quenching agent to hypochlorite required. Experiments were carried out in 13% hypochlorite and residual chlorine was measured using the DPD test. Sodium thiosulfate required the least number of moles to quench hypochlorite and was the most cost effective quenching agent ($0.11 per 10 mL of 13% hypochlorite). However due to potential interferences with the bromate analysis, sodium thiosulfate was removed from further consideration. Thus, malonic and oxalic acids remained as quenching agent candidates. Out of these two, malonic acid was the most cost-effective and required a smaller number of moles to quench sodium hypochlorite. Though costs were considered in this study for reference, it was not a major factor in the final choice of quenching agent.

Quenching Agent Decision Matrix

A generalized decision matrix is included in Table 2.4 with bold-faced text referring to reasons for rejecting a given quenching agent. Based on safety, ease of handling, transport, and stability, *glycine, hydrogen peroxide, sodium sulfite, and ascorbic acid were not recommended for quenching.* Based on negative impacts on bromate analysis, *ascorbic acid, sodium thiosulfate was not recommended for quenching.* Based on limited solubility of oxalic acid in bulk sodium hypochlorite solutions, *oxalic acid was not recommended for quenching.* Thus, malonic acid was chosen as the quenching agent of choice for experiments requiring preservation (typically for samples collected off-site and requiring shipping). For in-house experiments, the use of quenching agent was not required as the mass spectrometric and the titrimetric methods were not impacted by residual FAC; cooling the samples to 4 °C was sufficient to slow the reactions below appreciable levels if analyzed within a 3-month window.

Table 2.4
Summary of quenching agent test results and decision-making matrix

	Quenching Agent (QA)						
	Ascorbic Acid	Glycine	Malonic Acid	Sodium Thiosulfate	Sodium Sulfite	Oxalic Acid	Hydrogen Peroxide
Stoichiometric ratio of quenching agent to FAC*	1.2	0.55	0.75	0.28	1.1	1.5	1.1
Compatible with iodometric determination?	**No**	Yes	Yes	Yes	Yes	Yes	**No**
Effect on bromate	**Decrease**	No effect	No effect	**Decrease**	**Decrease**	No effect	No effect
Effect on perchlorate	No effect	No effect	No effect	No effect	No effect	No effect	No effect
Effect on chlorate	**High bias**	N/A	No change	No change	No change	No change	N/A
Cost per 100 g	$33.60	$43.00	$25.30	$11.72	$5.96	$27.90	$32.50 / 100mL 32% w/w
g to quench 10mL 13% hypochlorite	3.97	1.82	2.48	0.93	3.64	4.97	0.70
Cost to quench 10mL of 13% hypochlorite	$1.34	$0.78	$0.63	$0.11	$0.22	$1.39	$0.65
Solution stable over time	**No**	Yes	Yes	Yes	**No**	Yes	**No**
Any related safety issues?	No	**Violent reaction**	No	No	No	**Noxious gas evolved**	**Violent reaction, hazardous**
Requires additional reagents?	No	No	No	No	No	**NaOH**	No
Soluble in hypochlorite solutions?	Yes	Yes	Yes	Yes	Yes	**No**	Yes

*FAC = Free available chlorine as measured by DPD method; Bold-faced type represents reason for rejecting a g quenching agent

Validation of LC-MS/MS Method for the Analysis of Hypochlorite Solutions

Sodium hypochlorite solutions subjected for analysis ranged from 0.35 – 13%. Thus, a robust sample preparation method had to be identified in order to ensure accurate and reproducible detection of bromate, chlorate, and perchlorate. Furthermore, sulfate, known to occur in natural water, posed a potential source of isobaric interference to the analysis of perchlorate; as such, sulfate removal techniques (e.g., barium/hydrogen cartridge filters) were used initially on unknown (i.e., utility) samples until it could be determined by analysis of an unfiltered sample that no sulfate interference existed.

Analysis of hypochlorite and hypochlorite plus chlorate, bromate, and perchlorate spikes with and without sulfate removal steps were compared to validate the clean-up steps. Sample solutions were passed sequentially through one 2.5cc OnGuard II Ba and one 2.5cc OnGuard II H Cartridge (Dionex, Sunnyvale, CA) to reduce sulfate and carbonate ion concentrations. The cartridges were conditioned by flushing and discarding 30 mL deionized water. Sample solutions were eluted typically at a flow rate of 2.0 mL/min using mechanical syringe pump and at least the first 10 mL of eluent were discarded prior to collecting a sample aliquot for analysis. The results of dilutions on measured analyte concentration with and without the clean-up step are summarized in Tables 2.5 and 2.6. There were no major differences between filtered and unfiltered samples observed that could not be explained by the dilution effects discussed below. Thus, it was decided that if sulfate interference was possible, the use of a clean-up/filtration step with Barium cartridges would not negatively impact analysis.

Table 2.5
Measured analyte concentrations with and without filtration and at different dilutions (n = 3)

		ClO_3^- (mg/L)				BrO_3^- (µg/L)				ClO_4^- (µg/L)		
	Dilution factor	5000	1000	100	10	5000	1000	100	10	1000	100	10
Hypochlorite, no filtration	Analyte concentration	311	291	255	113	9017	8803	7433	509	3137	3303	3290
	Std. Dev.	3.3	9.5	4.9	1.5	340	110	275	71.9	35	85	26
	RSD	1.1	3.2	1.9	1.4	3.8	1.3	3.7	14.1	1.1	2.6	0.8
Hypochlorite with Ba/H filtration	Analyte concentration	308	287	257	93.2	9283	9117	8113	3973	3070	3253	3243
	Std. Dev.	4.8	11.2	2.1	5.7	126	275	146	601	61	68	60
	RSD	1.6	3.9	0.8	6.1	1.4	3	1.8	15.1	2	2.1	1.9

Table 2.6
Spike recoveries of analytes with and without filtration and at different dilutions (n = 3)

	Dilution factor	ClO_3^- 5000	ClO_3^- 1000	ClO_3^- 100	BrO_3^- 5000	BrO_3^- 1000	BrO_3^- 100	BrO_3^- 10	ClO_4^- 1000	ClO_4^- 100	ClO_4^- 10
Hypochlorite, no filtration	% Recovery	91	200	42	100	94	86	7.7	99	96	95
	Std. Dev.	11.4	42.3	15.3	2.3	2.5	17.2	0.8	2.3	4.6	5.1
	RSD	12.5	21.7	36.4	2.2	2.7	20	10.7	2.4	4.8	5.4
Hypochlorite with Ba/H filtration	% Recovery	98	230	8.1	99	90	89	-16	100	100	100
	Std. Dev.	10.2	25.6	10.7	5.9	6.8	3.5	40.8	3.5	2.3	3.9
	RSD	10.5	11.3	132.3	6	7.5	4	250.4	3.3	2.3	3.9

In addition to the clean-up and filtration tests, a series of dilution tests were also completed in order to examine the impact of other matrix interferences (e.g., ion suppression, ion enhancement, isobaric interferences, chromatographic resolution). The analysis of perchlorate was the least impacted by sample dilution with matrix recoveries hovering around 100% for all dilutions and analyte concentrations remaining within 3% regardless of dilution factor. Thus, perchlorate analysis was able to be performed at dilutions as low as 1:10, achieving a lower MRL than originally proposed. Chlorate was typically present at levels approaching the g/L range, requiring dilutions of several orders of magnitude. Analysis of bromate was the most susceptible to the matrix effects. Interestingly, the loss in signal of the ^{18}O-labeled bromate was much higher than that of the analyte at 1:10 and 1:100 dilutions. At a 1:1000 dilution, peak-widening was significantly reduced and showed no effect on the accuracy. Examples of the chromatograms of bromate ion signal are shown in Figures 2.7 – 2.9. At a 1:100 dilution, however, the bromate peak appears to be reasonably resolved, yet the ^{18}O-labeled bromate internal standard peak is significantly impacted by matrix interferences, thereby producing an erroneous result. A higher dilution eliminated this problem. In most cases, the sensitivity of the LC-MS/MS method allowed matrix effects to be minimized by diluting the samples. Fig. 2.10 illustrates the improvement in accuracy of the analytes based on the dilution factor.

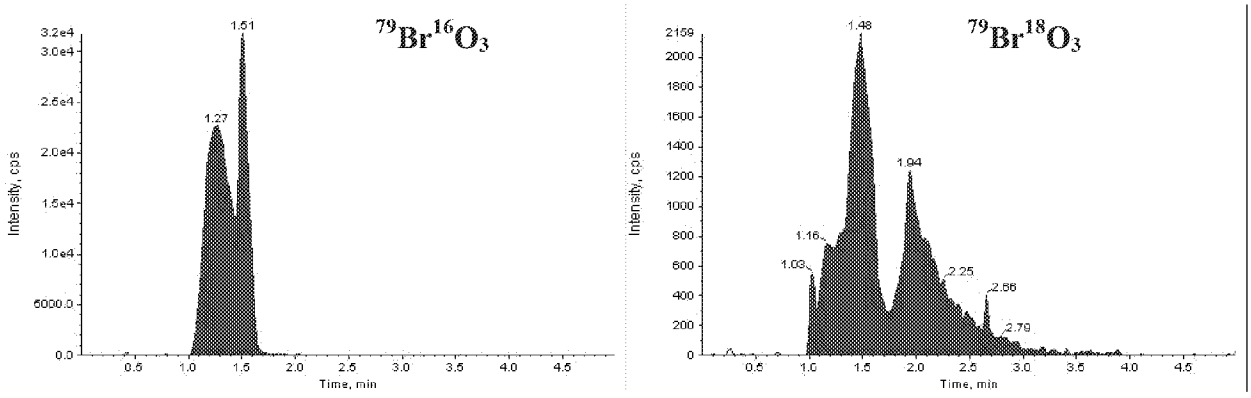

Figure 2.7 Bromate chromatogram of a sample diluted by a factor of 1:10

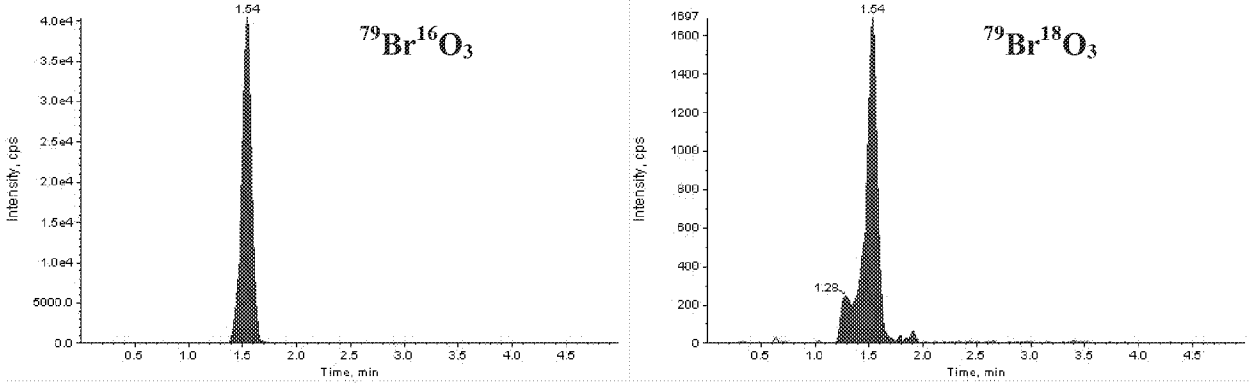

Figure 2.8 Bromate chromatogram of a sample diluted by a factor of 1:100

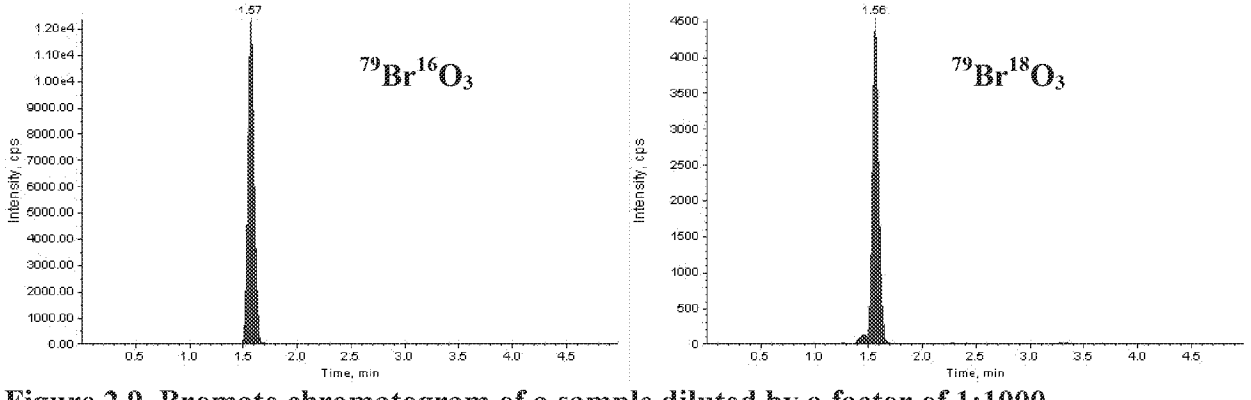

Figure 2.9 Bromate chromatogram of a sample diluted by a factor of 1:1000

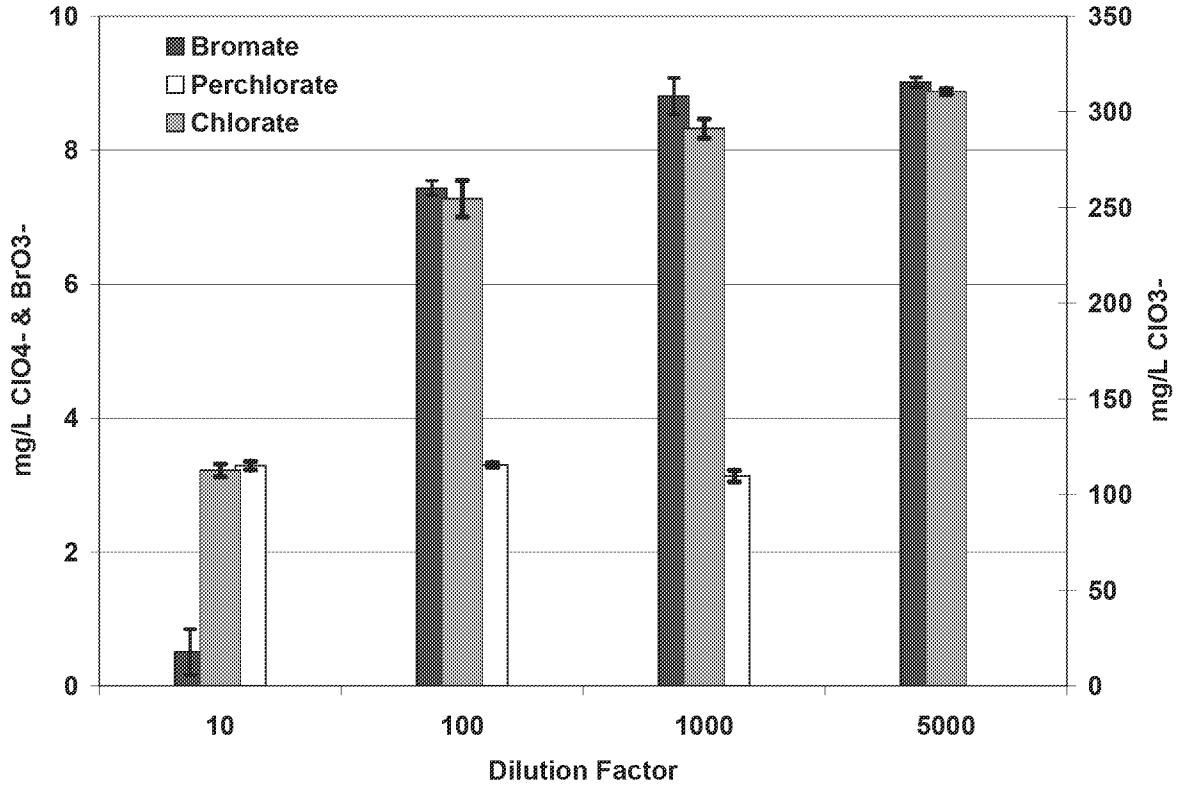

Figure 2.10 Sample concentrations of analytes measured at different dilutions

Comparison of LC-MS/MS and Titrimetric Methods: Selection Criteria for Sample Analysis

Sodium hypochlorite solutions are provided as either bulk, which is commercially available 6.5-13% as Free Available Chlorine (FAC), or as On-site Generated NaOCl that typically is 0.3-3% as FAC. Concentration of chlorate in some bulk hypochlorite samples was present at 200 g/L, thus dilutions on the order of 1:1,000,000 were needed for the LC-MS/MS analysis. In OSG hypochlorite, chlorate concentrations were typically below 1 g/L, which proved difficult to measure by iodometric titration. To determine which method (iodometric titration or LC-MS/MS) was best for chlorate analysis of either bulk or OSG sodium hypochlorite solutions, replicate samples were split and analyzed by both methods and their results compared. A comparison of the two methods for analysis of seven replicate bulk hypochlorite solutions is shown in Table 2.7.

Table 2.7
Data from the analysis of 7 replicate bulk hypochlorite solutions (13 % FAC) by LC-MS/MS and titration methods

	Unspiked hypochlorite		ClO_3^- spiked hypochlorite		% Recovery	
Replicate	LC-MS/MS	Titration	LC-MS/MS	Titration	LC-MS/MS	Titration
1	16.9	17.7	24.4	25.2	95.7	95.1
2	18.0	17.9	24.4	24.8	81.7	88.3
3	15.9	17.7	23.5	25.2	97.0	95.1
4	15.4	17.7	23.1	25.0	98.3	92.8
5	16.1	17.9	25.1	25.2	115	92.8
6	12.9	17.9	24.0	25.2	142	92.8
7	16.5	18.1	23.0	25.4	83.0	92.8
Mean	**16.0**	**17.9**	**23.9**	**25.1**	**102**	**92.8**
Std. Dev.	1.6	0.1	0.8	0.2	20.8	2.3
RSD	**9.9**	**0.8**	**3.2**	**0.7**	**20.4**	**2.4**

These results indicate that, although both methods produce similar results, titration of the concentrated hypochlorite solutions resulted in much lower relative standard deviations (RSD) than the LC-MS/MS method. The higher variability observed in the LC-MS/MS results are most likely a result of the number of dilutions in order to bring 10 – 200g/L concentrations down to the calibration curve of 5 – 500 µg/L or a dilution factor of up to 1,000,000. Carrying out serial dilutions of several orders of magnitude may have compounded errors associated with each dilution made resulting in higher variability. This variability can be visually observed from the comparison of the results from two methods of duplicate samples during a chlorate-spike experiment, shown in Fig. 2.11. It should be noted that in this context connecting lines were used for visual impact. However, in all other figures (unless otherwise noted), best-fit lines are used.

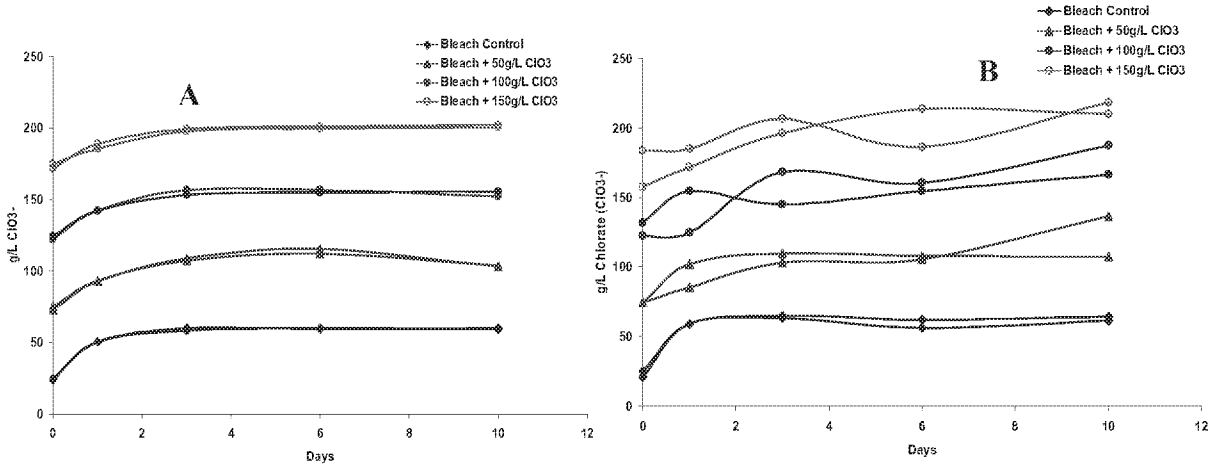

Figure 2.11 Comparison of chlorate ion concentrations measured by titration (A) and by LC-MS/MS (B) during a chlorate-spike experiment

Given these results, the iodometric titration method was used for the vast majority of bulk hypochlorite samples for the determination of chlorate ion concentration. However, for the analysis of OSG hypochlorite, the titration method could not be used as reliably. The results shown in Table 2.8 indicate poor precision for determination of chlorate at concentrations less than 1.0 g/L (10 mM).

Table 2.8
Data from the analysis of replicate OSG hypochlorite solutions with concentration of ClO_3^- at less than 1.0 g/L (< 10 mM) by iodometric titration and LC-MS/MS methods

	Titration	LC-MS/MS
Mean	**0.560**	**0.31**
Std. Dev.	0.20	0.005
RSD (%)	35.23	1.55
	(n=4)	(n=3)

Results are in g/L ClO_3^-

The iodometric determinations of chlorate concentrations at less than 1 g/L were unreliable, thus requiring analysis by LC-MS/MS. Therefore, chlorate measurements for samples from bulk hypochlorite were analyzed by iodometric titration while OSG hypochlorite solutions were analyzed by LC-MS/MS. Specifically, the iodometric titration method was used for determination of chlorate concentrations in 10 – 250 g/L range (generally in hypochlorite solutions with >5% FAC), while LC-MS/MS method was used for trace chlorate analysis in the 0.01 – 10,000 mg/L range (generally in hypochlorite solutions with <5% FAC).

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CHAPTER 3
FACTORS IMPACTING PERCHLORATE FORMATION

BACKGROUND

The kinetics of the decomposition of the hypochlorite ion and subsequent formation of chlorite and chlorate ions in hypochlorite solutions has been well described and was the basis for much of the experimental design for this study (Gordon, et al. 1993; Adam 1994; Adam and Gordon 1995; Gordon, Adam, and Bubnis 1995; Gordon, et al. 1997; Adam and Gordon 1999). The results of the aforementioned research formed the underpinnings of the *Bleach 2001* predictive model (Adam, Gordon, and Pierce 2001), designed for bulk hypochlorite solutions in the pH range of 11 to 14 and for storage conditions with temperatures from 0 °C to 50 °C. The narrow pH range defined in the model is due to the fact that (1) the mechanism for hypochlorite ion decomposition is different (and the rate faster) at or below pH 10.5 and (2) most bulk hypochlorite samples used by drinking water utilities fall within the pH 11 – 14 range. The exception, of course, would be OSG hypochlorite which typically fall within the pH 9 – 10 range. The lack of applicability of the *Bleach 2001* model to OSG hypochlorite is less of a concern, however, as such solutions are typically used immediately, or at most within 48 to 72 hours of production. Thus, the work carried out for this current research study was designed around the use of bulk hypochlorite solutions in the pH 11 to 14 range in order to elucidate the mechanism of perchlorate formation.

Upon commencement of the research for this study the following facts were known about the chemistry of sodium hypochlorite solutions (Adam 1994):

1. Hypochlorite ion can decompose in the pH 11 – 14 range to form chlorate and chloride (Equation 1.1, Chapter 1) or, in the presence of a catalyst, oxygen gas and chloride (Equation 1.2, Chapter 1).

2. The rate law defining the decomposition of the hypochlorite ion in the pH 11 – 14 is defined by second order decomposition (Equation 1.3, Chapter 1).

3. The decomposition of the hypochlorite ion concomitantly results in the production of an intermediate species, the chlorite ion, which essentially remains at steady state during the production of chlorate ion.

4. The ionic strength of the hypochlorite solution impacts the rate of hypochlorite ion decomposition and subsequent chlorate ion formation; higher ionic strength favors faster reaction rates. The relationship between ionic strength, observed rate constant (k_{obs}), and the rate constant for infinite dilution (k_0, for 'zero' ionic strength) is defined by Equation 3.1.

$$\log k_{obs} = 0.149(I) + \log k_0 \qquad \textbf{(3.1)}$$

5. The pH of the hypochlorite solution impacts the rate of hypochlorite ion decomposition and chlorate ion formation; this reaction is minimized in the pH

11.86 – 13.00 region. At pH 14, the excess hydroxide ions contribute to the ionic strength, thereby also increasing the rate of reaction by a factor of 1.5 above that observed at pH 13.

6. Diluting hypochlorite solutions by a factor of two reduces the concentration of hypochlorite ion and ionic strength resulting in nearly a five-fold decrease in the rate of decomposition

7. The rate of hypochlorite ion decomposition increases proportionally with temperature and can be related to the zero ionic strength rate constant using the enthalpy ($\Delta H^{\ddagger}$) and entropy ($\Delta S^{\ddagger}$) of activation (Equation 3.2).

$$k_0 = 2.083 \times 10^{10} (T) \times e^{(-\Delta H^{\ddagger}/RT)} \times e^{(\Delta S^{\ddagger}/R)} \quad \textbf{(3.2)}$$

   By storing hypochlorite solutions at 15 °C instead of 25 °C, the rate of decomposition decreases by a factor of 3.8; Cooling from 35 °C to 15 °C decreases the rate of decomposition by a factor of 14.

8. Hypochlorite ion decomposition is not impacted by the presence of carbonate or sulfate ions.

9. The presence of some transition metal ions catalyzes the decomposition of hypochlorite ions. Fe(III) and Mn(II) were shown to have no effect at concentrations of 1.1 mg/L for Mn(II) and 42 mg/L for Fe(III). Ni(II) present at 1 mg/L was able to increase the rate constant by a factor of 10, while Cu(II) at the same concentration only increased the rate constant by a factor of 1.4. However, at 10 mg/L, Cu(II) was able to increase the rate constant by a factor of 18.

With the facts listed above in mind, several hypotheses were developed to guide the experimental design:

1. The formation of perchlorate ion is a direct result of reactions between hypochlorite and chlorate ions in the following, generalized reaction:

$$OCl^- + ClO_3^- \rightarrow ClO_4^- + Cl^- \quad \textbf{(3.3)}$$

   What was not clear, however, was the reaction order with respect to hypochlorite and chlorate ions, though it was hypothesized that the reaction would be first order in both chlorate and hypochlorite.

2. The chlorite ion, given its steady state concentration, is not likely to impact the rate of formation of perchlorate ion.

3. The presence of bromide and bromate ions will not impact the rate of formation of perchlorate ion given that bromide and bromate ions are generally present at low concentrations relative to chloride and chlorate ions.

4. Temperature and ionic strength were hypothesized to impact the rate of perchlorate ion formation in a manner analogous to that of the decomposition of hypochlorite ion and subsequent formation of chlorate ion.

5. Higher initial concentrations of hypochlorite and chlorate ions were hypothesized to increase the rate of perchlorate ion formation.

6. The role of pH is likely to be significant in perchlorate ion formation. However, given the goal of predicting perchlorate formation in bulk hypochlorite, the pH ranges suggested in the experimental design were generally in the pH 11 – 14 range.

7. The presence of transition metal ions was hypothesized to impact the rate of perchlorate ion formation, though it was unclear whether the effect would enhance or retard the rate of formation.

APPROACH

Given each of the considerations and hypotheses listed above, a series of incubation studies on commercially available sodium hypochlorite solutions were carried out in the laboratory. Two hypochlorite suppliers were used: 13% FAC from Acros Organics USA (Morris Plains, NJ) and 10–14% w/w from VWR (Brisbane, CA). Analog and digital, general-purpose, heated water baths (VWR, Brisbane, CA) were used for incubations at 30, 40, 50, 60, and 76 °C. Temperatures were monitored daily, using glass laboratory mercury thermometer or a thermocouple thermometer with an LCD screen (Fisher Scientific, Pittsburgh, PA). Potassium bromide, Certified ACS grade (Fisher Scientific, Pittsburgh, PA); sodium bromate, 99.5% min (EMD Chemicals Inc., Gibbstown, NJ); sodium chlorate, ACS Grade, ≥99% pure (VWR, Brisbane, CA); and sodium chlorite, unstabilized, Technical Grade 80% (Acros Organics USA, Morris Plains, NJ) were added to sodium hypochlorite solutions to investigate individual and combined effects of contaminants on the decomposition of hypochlorite, formation of bromate, chlorate, and perchlorate. To adjust the pH of the sodium hypochlorite solutions, sodium hydroxide (reagent grade, ≥98%, pellets, Sigma-Aldrich, St. Louis, MO) and hydrochloric acid (ACS reagent, 37%, Sigma-Aldrich, St. Louis, MO) were used. To investigate the effects of metal ions, aliquots of 1,000 ppm Co, Cu, Fe, Ni, and Mn Standards (SPEX CertiPrep®, Inc., Metuchen, NJ) and 1,000ppm Ag, Au, Ir, Pd, and Pt Standards (Elements Inc., Shasta Lake, CA) were spiked into sodium hypochlorite solutions. Dilutions of the sodium hypochlorite solutions and preparation of standards was performed using reagent water purified using Milli-Q Gradient System (Millipore, Billerica, MA). In order to investigate factors that impact perchlorate formation, over 1,600 sample titrations and 1,600 LC-MS/MS data points were collected (not including standardization titrations and calibrations).

INVESTIGATION OF FACTORS IMPACTING PERCHLORATE FORMATION

Part of the challenge faced in designing this research study was how best to design the experiments to provide the amount of information required to determine a chemical rate law within the 9 month time line. Given the short duration of the study, the decision was made that multiple factors would need to be investigated simultaneously while still ensuring that the proper

controls were in place to elucidate individual effects. Thus, at the end of the experimental phase of the study, a significant amount of deconvolution of factors/effects was required. Using the data collected from the experiments designed for this study, the individual effects of oxychloride ion concentration, bromide and bromate concentrations, metal ion concentration, ionic strength (using conductivity as a surrogate measure to calculate ionic strength), temperature, and pH were discernable. However, in presenting the results, the reader may notice some overlap between the sections and/or find questions that are raised in one section but are not fully answered until a later section. To keep this to a minimum, the factors impacting the rate of perchlorate formation are presented in the following order: hypochlorite and chlorate ion concentration effects, chlorite ion effects, metal ion effects, bromide and bromate ion effects, temperature, ionic strength, and pH.

Effects of Hypochlorite Ion and Chlorate Ion Concentrations on the Rate of Perchlorate Formation

To investigate effects of chlorate and hypochlorite ions on perchlorate formation, solutions of sodium hypochlorite were spiked with variable amounts of chlorate and hypochlorite ions and incubated at 30, 40, and 50 °C for periods of up to 200 days. The samples were divided into three unique sets and labeled as follows:

- Constant hypochlorite concentration with variable chlorate concentrations
- Constant chlorate concentrations with variable hypochlorite concentrations
- A constant mole product of [hypochlorite] x [chlorate]

The use of sodium hypochlorite solutions with constant [OCl^-] and variable [ClO_3^-] were used to elucidate the order of the rate of perchlorate formation with respect to chlorate ion. Similarly, solutions with constant [ClO_3^-] and variable [OCl^-] concentrations were used to determine the order with respect to hypochlorite. Should the results indicate that the formation of perchlorate is first order in hypochlorite and first order in chlorate, the constant mole product results would be expected to form the same amount of perchlorate over the incubation period. Given the hypothesis that the initial rate of reaction is first order in chlorate and first order in hypochlorite (thus second order overall), the following rate law equation was proposed:

$$\frac{d[ClO_4^-]}{dt} = k_2[ClO_3^-]^m[OCl^-]^n \qquad \textbf{(3.4)}$$

Where k_2 = the apparent second order rate constant and m and n are approximately 1.

Constant Hypochlorite with Variable Chlorate at 30, 40, and 50 °C

In this set of experiments, hypochlorite solutions were prepared having the same starting hypochlorite ion concentration[1], while additional chlorate ion was spiked at 50 g/L, 100 g/L, and

[1] As a point of reference for discussion, a bulk hypochlorite solution of 13% FAC equates to approximately 2 M OCl^-, 103 g/L OCl^-, 149 g/L NaOCl, and/or 13.6% NaOCl (depending on specific gravity).

150 g/L. A control solution containing no additional chlorate ion above the background was also included. All samples were incubated in duplicate. The results presented in Figures 3.1 demonstrate the effects of different initial chlorate ion concentrations on formation of perchlorate ion at 30 °C (a), at 40 °C (b), and at 50 °C (c). The results presented in Figures 3.2 demonstrate the effects of different initial chlorate ion concentrations on the decomposition of hypochlorite ion and formation of chlorate ion at 30 °C (a), at 40 °C (b), and at 50 °C (c). The addition of chlorate to the hypochlorite solution causes a proportionate increase in perchlorate, confirming that changes in initial chlorate ion concentration affect the rate of formation of perchlorate. Casual observation of the results would point toward a reaction mechanism that is first order in chlorate (this is elucidated in more detail later).

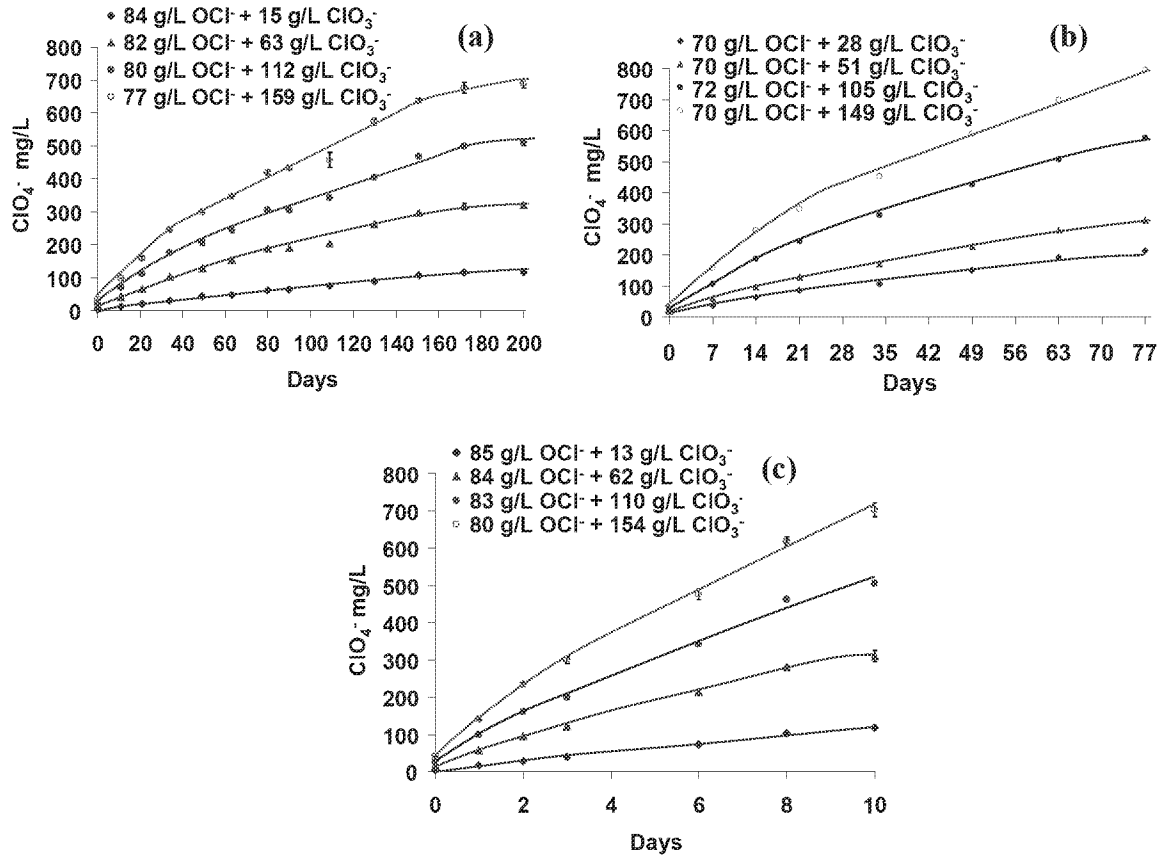


Figure 3.1 Formation of perchlorate as measured by LC-MS/MS for constant hypochlorite / variable chlorate, at (a) 30 °C, (b) 40 °C , and (c) 50 °C

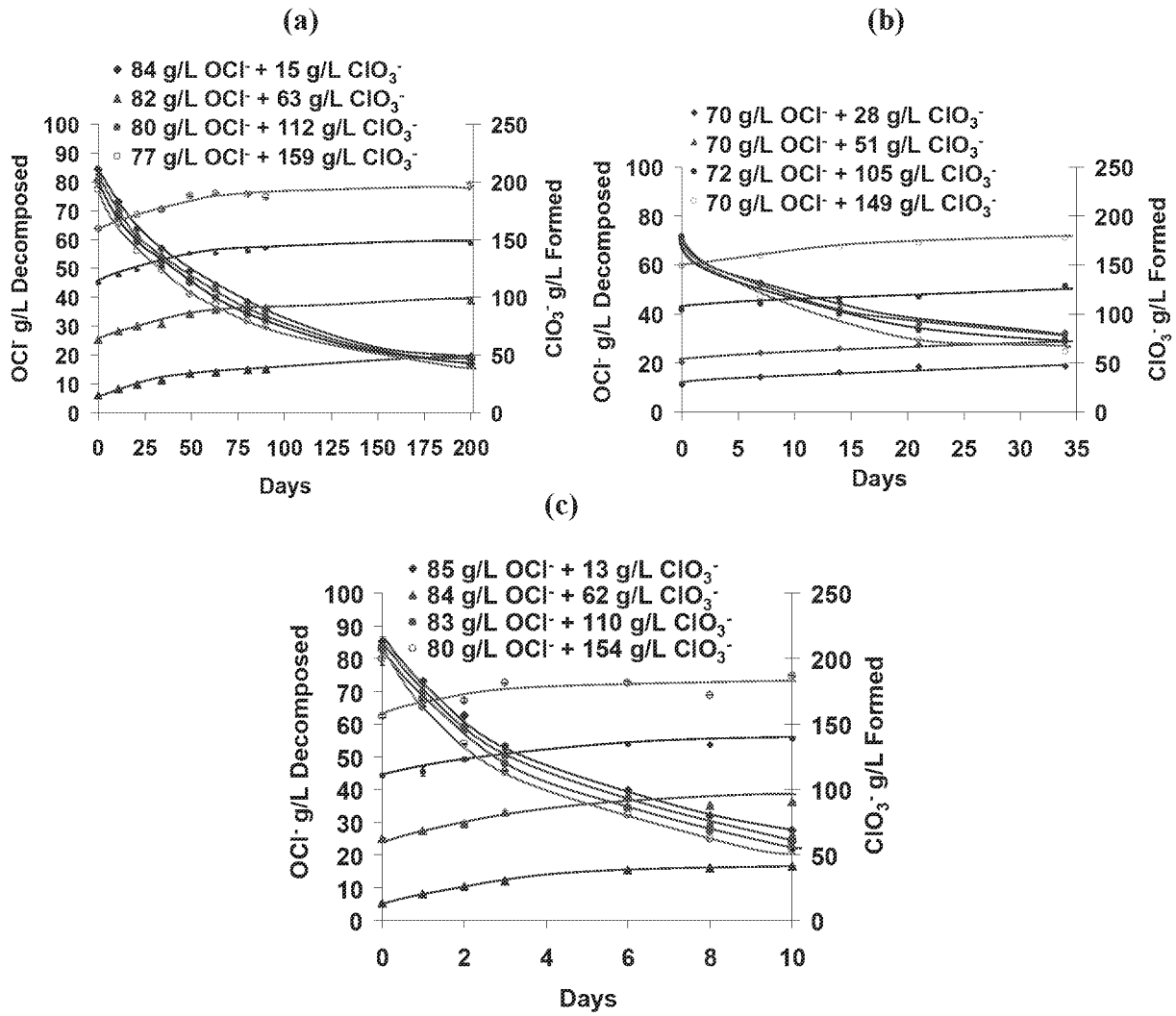


Figure 3.2 Decomposition of hypochlorite and formation of chlorate as measured by titration for constant hypochlorite/variable chlorate, at (a) 30 °C, (b) 40 °C (c) 50 °C

Constant Chlorate/Variable Hypochlorite at 30, 40, and 50 °C

Similar to the effects of variable chlorate ion concentration, the results of this data set provide evidence that changes in hypochlorite ion concentration also affects the rate of formation of perchlorate. Here, hypochlorite ion concentration was varied by dilution while appropriate amounts of sodium chlorate were added to keep chlorate ion concentration the same for all samples. Typically three or more hypochlorite ion concentrations were studied. Figure 3.3 shows plots of average concentrations of perchlorate ion (based on duplicate samples) at different temperature and associated errors of measurements at each temperature. The results presented in Figures 3.4 demonstrate the effects of different initial chlorate ion concentrations on the decomposition of hypochlorite ion and formation of chlorate ion at 30 °C (a), at 40 °C (b), and at 50 °C (c). Similar to chlorate ion involvement, hypochlorite ion is also involved in formation of perchlorate; samples containing lower hypochlorite ion concentrations show less perchlorate formed.

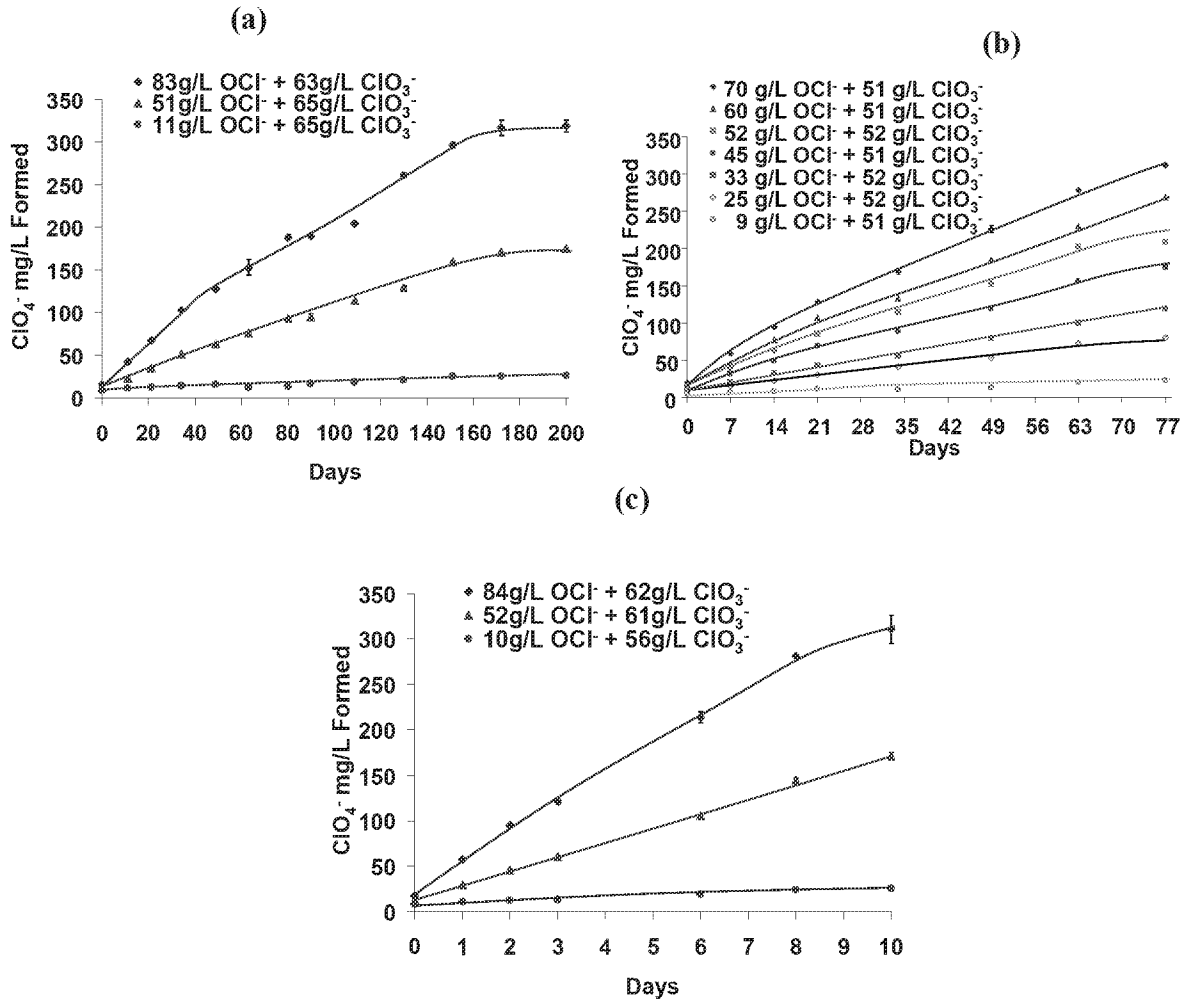


Figure 3.3 Formation of perchlorate as measured by LC-MS/MS for variable hypochlorite, constant chlorate, at (a) 30 °C, (b) 40 °C, and (c) 50 °C

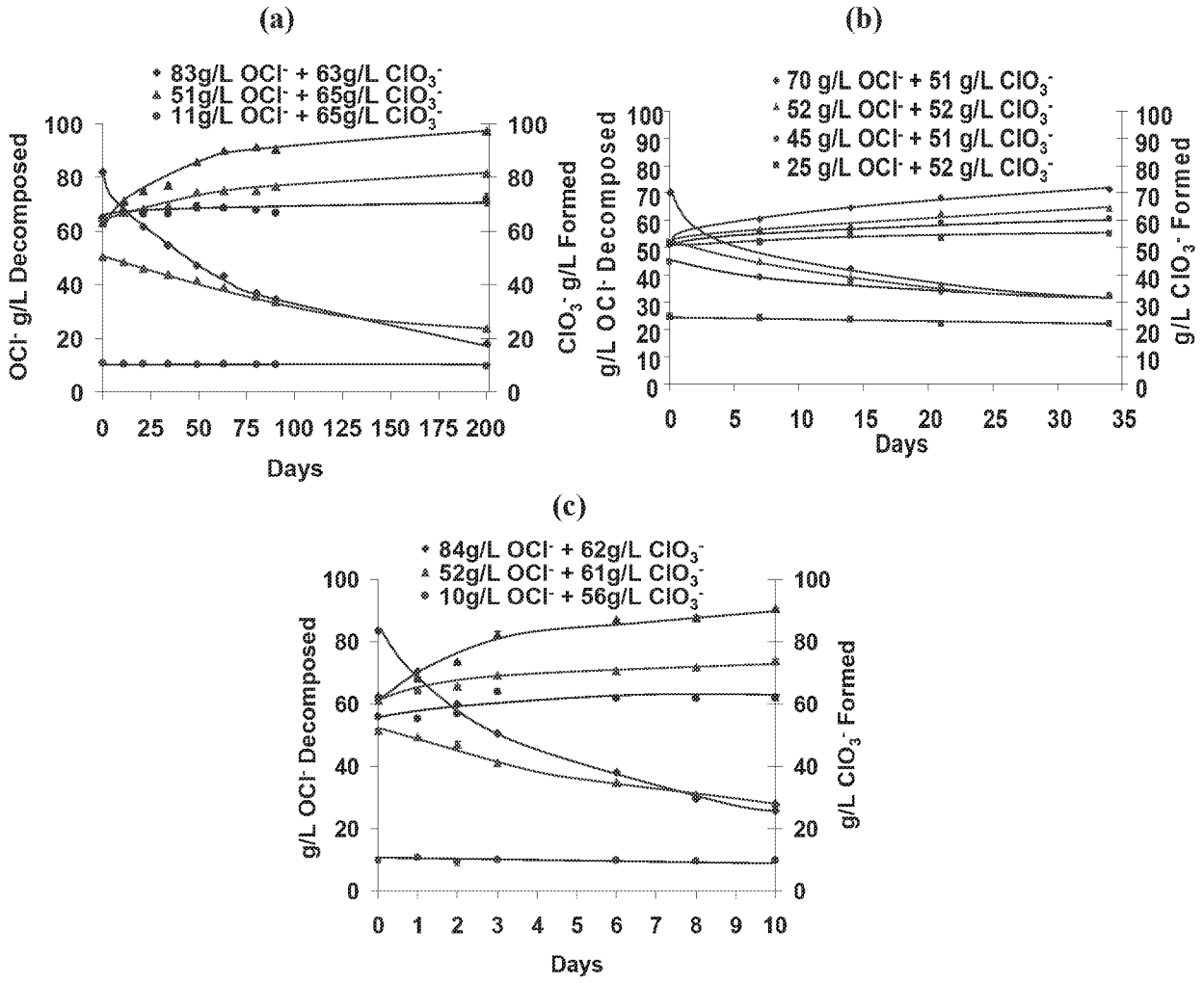


Figure 3.4 Decomposition of hypochlorite and formation of chlorate as measured by titration for variable hypochlorite / constant chlorate, at (a) 30 °C, (b) 40 °C, and (c) 50 °C

Constant Molar Product of [Hypochlorite] x [Chlorate]

Because the rate of perchlorate formation appeared to be first order in chlorate and hypochlorite ions, it was expected that when the molar product was kept constant, the same rate of perchlorate formation would be observed between samples. Both hypochlorite and chlorate ion concentrations were varied in such a way that the molar product was kept constant (1.9% RSD for 30 °C set and 13.4% RSD for 50 °C) and the samples were incubated at 30 °C and 50 °C. Figure 3.5 shows plots of average concentration of perchlorate ion (based on duplicate samples) and associated errors of measurements at each temperature. Figure 3.6 shows the decomposition of hypochlorite ion and formation of chlorate ion at each temperature.

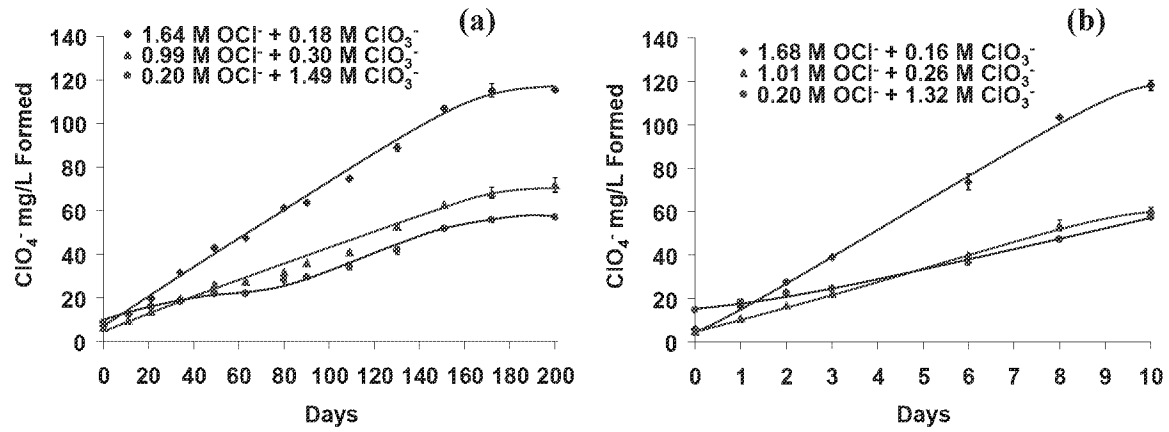


Figure 3.5: Formation of perchlorate as measured by LC-MS/MS for constant [OCl^-] x [ClO_3^-], (a) 30 °C, (b) 50 °C

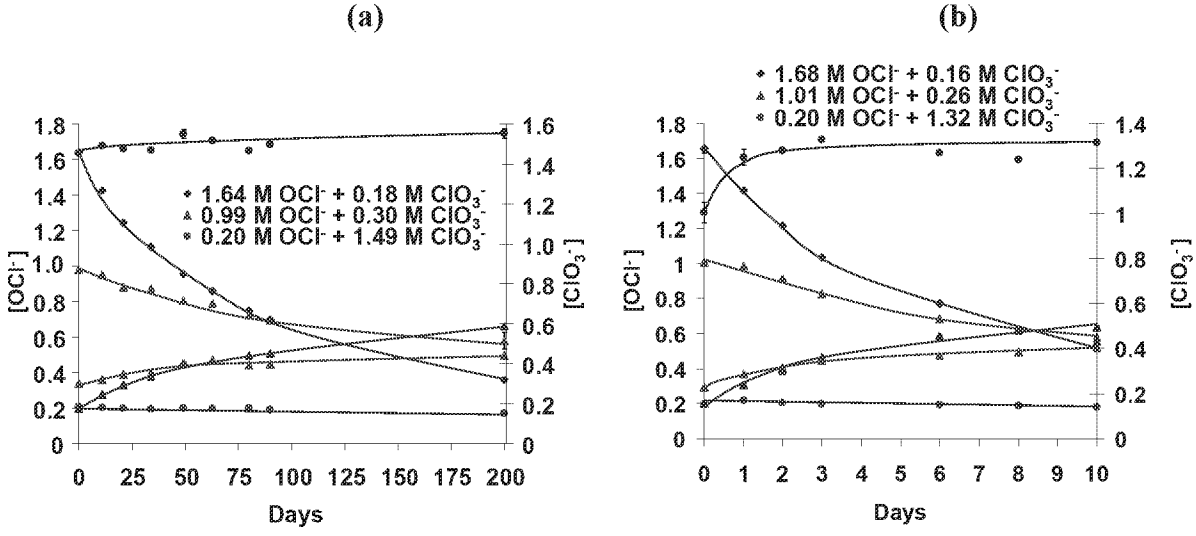


Figure 3.6 Decomposition of hypochlorite and formation of chlorate as measured by titration for constant [OCl^-] x [ClO_3^-], (a) 30 °C, (b) 50 °C

It is immediately evident from Figure 3.5 (a, b) that the assumption of first order in both hypochlorite ion and chlorate ion may have been incorrect OR that other factors (e.g., ionic strength, pH) may have been impacting the results. More perchlorate ion was formed in the sodium hypochlorite solution having higher initial hypochlorite ion concentration than those with lower concentration. The test solutions with higher initial hypochlorite ion concentration appeared to produce similar perchlorate ion concentration initially but began to deviate with time (Figure 3.6). To verify that the samples were indeed constant in molar product of [OCl^-] and [ClO_3^-], the measured concentrations were used to calculate the changes in molar product over time. Changes in the molar product of hypochlorite and chlorate ions over the experimental incubation period are listed in Tables 3.1 and 3.2, while the data are presented graphically in Figure 3.7.

Table 3.1
Changes in constant-molar-product experiments over incubation period at 30 °C

Day	$[OCl^-]x[ClO_3^-]$: 1.64 M x 0.18 M	$[OCl^-]x[ClO_3^-]$: 0.99 M x 0.30 M	$[OCl^-]x[ClO_3^-]$: 0.20 M x 1.49 M
0	0.291	0.295	0.302
11	0.347	0.303	0.302
21	0.362	0.303	0.295
34	0.372	0.307	0.284
49	0.385	0.326	0.304
63	0.360	0.327	0.301
80	0.328	0.284	0.290
90	0.315	0.276	0.284
200	0.210	0.254	0.261

Table 3.2
Changes in constant-molar-product experiments over incubation period at 50 °C

Day	$[OCl^-]x[ClO_3^-]$: 1.68M x 0.16 M	$[OCl^-]x[ClO_3^-]$: 1.01M x 0.26 M	$[OCl^-]x[ClO_3^-]$: 0.20 M x1.32 M
0	0.258	0.230	0.197
1	0.336	0.284	0.276
2	0.381	0.276	0.262
3	0.376	0.286	0.260
6	0.352	0.253	0.246
8	0.297	0.240	0.235
10	0.266	0.234	0.240

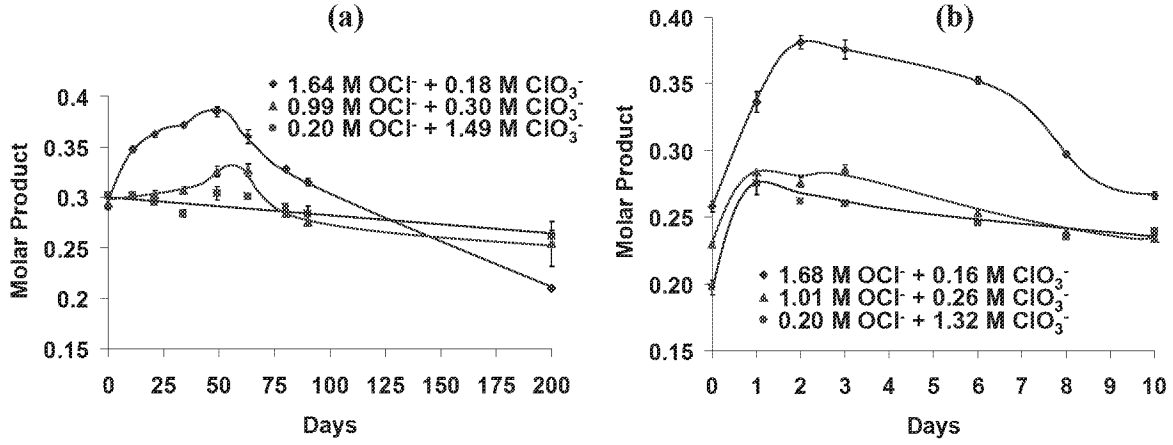


Figure 3.7 Changes in molar product of $[OCl^-]$ x $[ClO_3^-]$ (a) 30 °C, (b) 50 °C

The discrepancy in the perchlorate ion formation results between the three sets of constant molar-product experiments and the fact that initial molar products were within 10% suggests several possibilities: (1) The order with respect to hypochlorite may be higher than one. This can be inferred in part from the observation that in the two lowest [OCl^-] concentration samples, the changes in molar product were in better agreement than the high [OCl^-] concentration sample. Such a result suggests a dependence on hypochlorite ion concentration which is different from the dependence on chlorate ion. Thus, the order of perchlorate formation may still be one with respect to chlorate. (2) The rate of perchlorate formation may be dependent on another variable not considered during the initial design of the constant-molar-product experiments. One would expect that as a concentrated sodium hypochlorite solution is diluted (even with subsequent addition of sodium chlorate), the ionic strength and/or pH would also change. Indeed this was the case: Table 3.3 shows the ionic strength variance with dilution of the stock concentrated sodium hypochlorite solution. While pH did not vary by more than 0.8 pH units, the ionic strength varied by nearly 3 fold during dilution. Thus, ionic strength was suspected as an important factor in determination of the rate law for perchlorate formation.

Table 3.3
Ionic strength and constant-molar-product experiments at 30 and 50 °C

30 °C Experiment:	[OCl^-]	[ClO_3^-]	Ionic strength (M)		pH
[OCl^-]x[ClO_3^-]: 1.64M x 0.178M	1.637	0.178	6.50		12.88
[OCl^-]x[ClO_3^-]: 0.986M x 0.298M	0.977	0.302	4.23		12.69
[OCl^-]x[ClO_3^-]: 0.197M x 1.49M	0.209	1.454	2.86		12.13
				Mean	12.57± 0.39
50 °C Experiment:					
[OCl^-]x[ClO_3^-]: 1.68M x 0.158M	1.658	0.156	6.31		12.89
[OCl^-]x[ClO_3^-]: 1.01M x 0.264M	1.008	0.228	4.20		12.69
[OCl^-]x[ClO_3^-]: 0.202M x1.32M	0.196	1.006	2.66		12.11
				Mean	12.56± 0.41

Chlorite Ion Effects

Chlorite ion concentration typically reaches steady state in hypochlorite solutions and is an intermediate in the formation of chlorate (Lister 1956; Adam, et al. 1992; Adam and Gordon 1999). Thus, when sodium chlorite is added to a sodium hypochlorite solution, chlorite ions can be expected to react with hypochlorite to produce chlorate ions based on the reactions described in Equations 3.5 and 3.6:

$$OCl^- + OCl^- \longrightarrow ClO_2^- + Cl^- \qquad k_{ClO2-}(\text{slow}) \qquad \textbf{(3.5)}$$

$$OCl^- + ClO_2^- \longrightarrow ClO_3^- + Cl^- \qquad k_{ClO3-}(\text{fast}) \qquad \textbf{(3.6)}$$

To determine whether chlorite ion could represent an additional perchlorate ion formation pathway, chlorite ion was spiked at 15 g/L with and without an additional spike of chlorate ion at 100 g/L. Formation of perchlorate for the 30 °C and 50 °C incubation studies is shown in Figure 3.8. Figure 3.9 shows the change in perchlorate ion concentration overlaid with changes in the molar product at each temperature. Decomposition of hypochlorite ion overlaid with the formation of chlorate ion is shown in Figures 3.10. The data indicate the addition of chlorite ion does not appear to offer a substantial change in perchlorate formation beyond what would be observed from the addition of chlorate ion represented in Equations 3.5 and 3.6. This is especially evident when the molar product of chlorate and hypochlorite are considered (Figure 3.9 (a, b)), showing nearly identical changes over time.

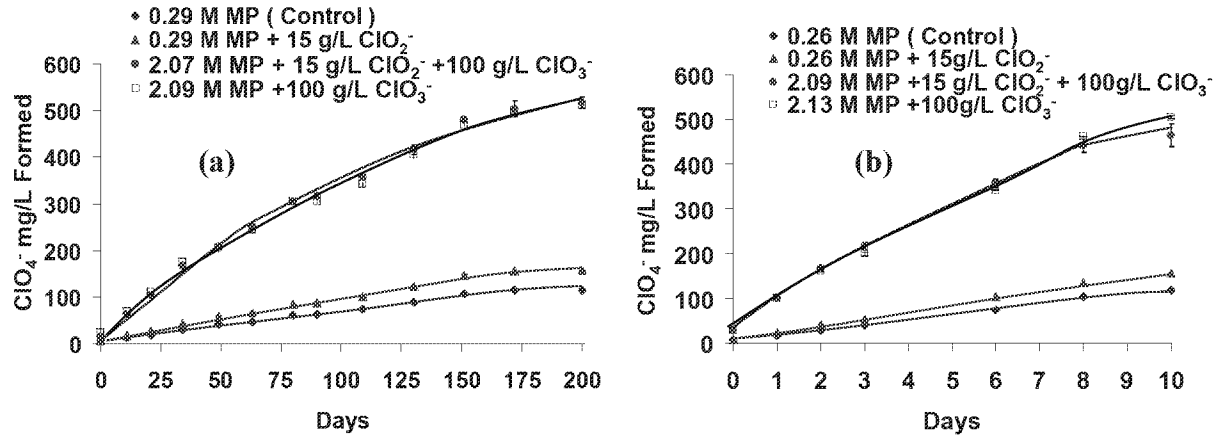


Figure 3.8 Formation of perchlorate measured by LC-MS/MS, effects of chlorite, (a) 30 °C, (b) 50 °C (MP = [OCl⁻]X[ClO_3^-])

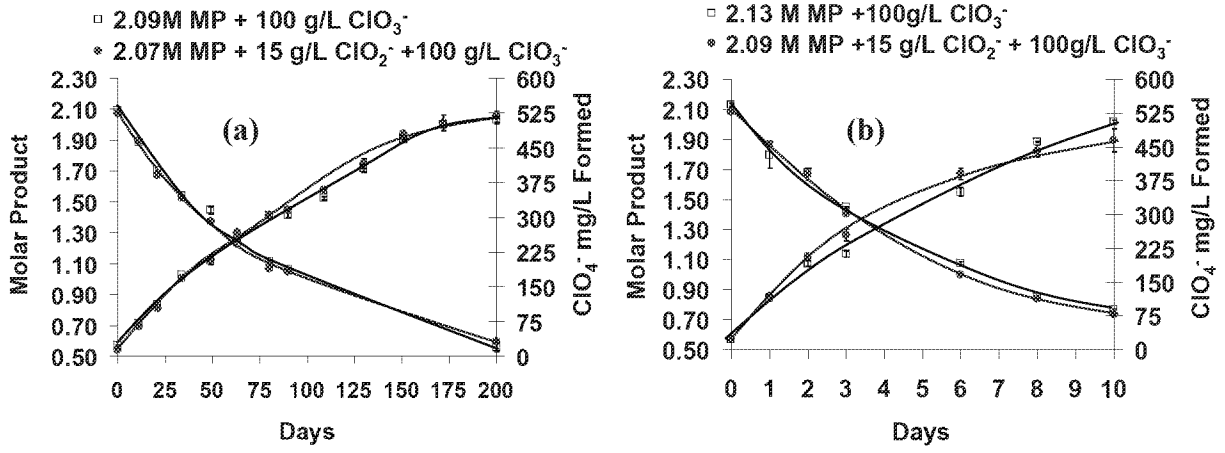


Figure 3.9 Comparison of changes in molar product (MP = [OCl⁻]X[ClO_3^-]) over time and the concomitant formation of perchlorate, effects of chlorite, (a) 30 °C, (b) 50 °C

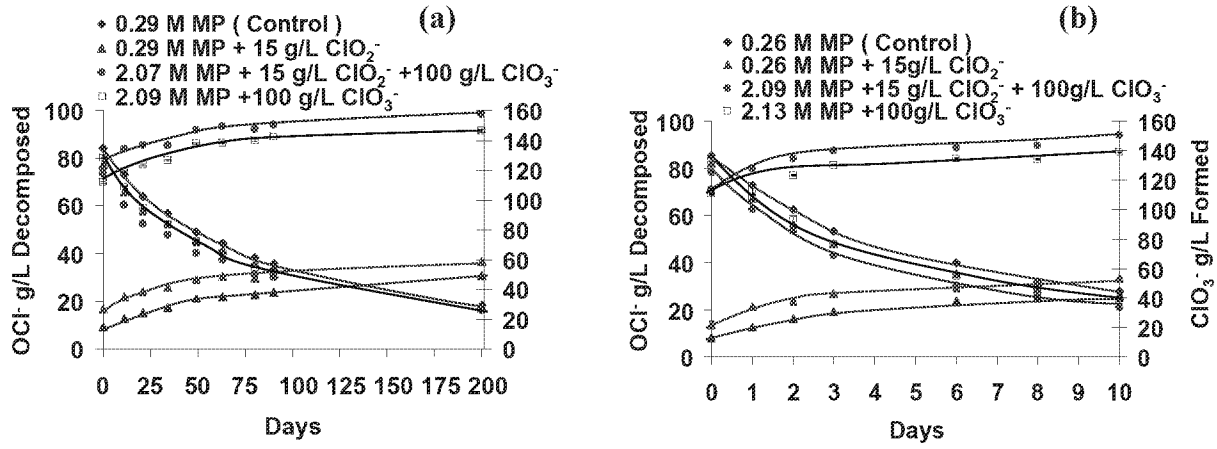


Figure 3.10 Decomposition of hypochlorite and formation of chlorate measured by titration effects of chlorite, (a) 30 °C, (b) 50 °C (MP = [OCl^-]X[ClO_3^-])

In summary, ClO_2^- reacts with OCl^- to form ClO_3^-, affecting the formation of ClO_4^- in two ways: The first effect is due to the conversion of chlorite ion to chlorate ion, enhancing the formation of perchlorate ion. The second effect, however, occurs at the same time whereby hypochlorite ion concentration is concomitantly reduced, thus decreasing the rate of formation of perchlorate ion. The combined outcome is that more perchlorate ion formation can be observed in chlorite ion-spiked hypochlorite solutions than control solutions. However, in samples spiked with both chlorite ion and high levels of chlorate ion, this effect is not as significant. The lower accumulation of perchlorate ion correlates to observed similarities in the molar product of the chlorate ion-spiked sample and chlorite/chlorate ion-spiked sample. The addition of chlorite ion does not enhance the rate of perchlorate ion formation mechanistically, however. Thus, it was determined that chlorite ion concentration was neither a significant factor in the kinetics of perchlorate ion formation nor in determination of the chemical rate law.

Metal Ion Effects

The potential catalytic effect of transition metal ions was initially investigated at 75 °C and evaluated the combined effects of Co^{2+}, Cu^{2+}, Fe^{3+}, Mn^{2+}, and Ni^{2+} at 20 mg/L final concentration. At this combination of temperature and concentration, the decomposition reaction of hypochlorite was too rapid to measure, and thus the effects (if any) of transition metals on the actual formation of perchlorate could not be observed. In a follow-up incubation study, 2 mg/L and 0.2 mg/L concentrations of metals were used in spiked hypochlorite solutions. Figure 3.11 (a) shows the concurrent loss of hypochlorite ion and formation of chlorate ion in the presence of transition metal ions. These results indicate that the metal ions catalyze a rapid decomposition of hypochlorite (as previously described by Adam 1994; Gordon, et al. 1997; Adam and Gordon 1999), overwhelming any possible effects that might have been observed during the catalysis of perchlorate formation. Therefore, rather than catalyzing perchlorate formation, the presence of the metal ions actually assist in the minimization of perchlorate ion formation at the expense of a loss of hypochlorite ion concentration in the hypochlorite solution as shown in Figure 3.11 (b).

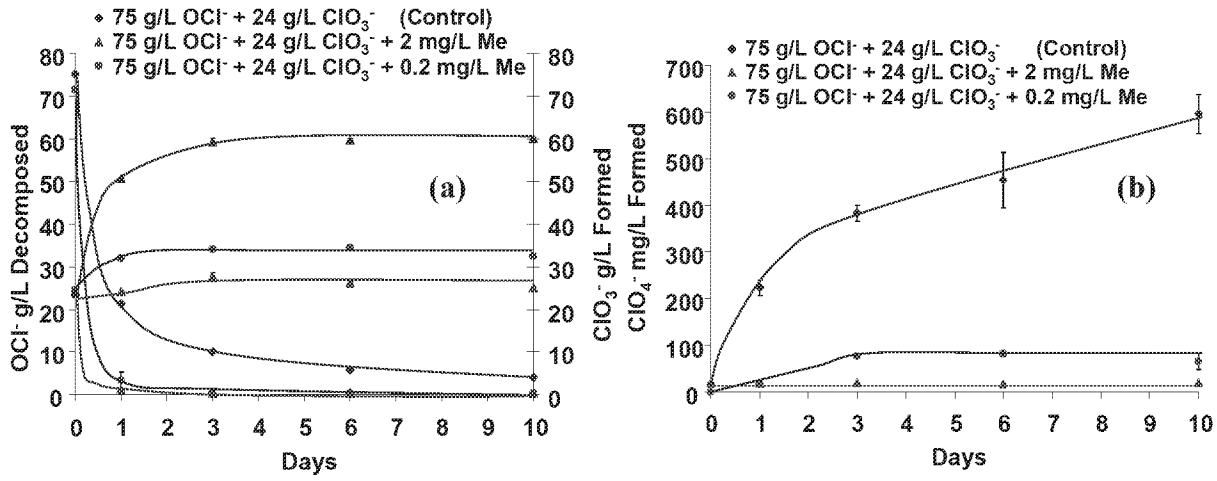


Figure 3.11 Effects of transition metals ions (Me = Co^{2+}, Cu^{2+}, Fe^{3+}, Mn^{2+}, Ni^{2+}): (a) decomposition of hypochlorite (downward sloping curves) & formation of chlorate (upper curves); (b) formation of perchlorate

The combined effects of chlorite ion, transition metals ions (Co^{2+}, Cu^{2+}, Fe^{3+}, Mn^{2+}, and Ni^{2+}), and bromide ion on formation of perchlorate and chlorate were also investigated by incubating liquid hypochlorite samples at 50 °C with the following amounts of chlorite ion, chlorate ion, and/or transition metal ion spikes, in duplicate:

Spike 1: ClO_2^- at 15 g/L + Transition Metals Spike at 0.2 mg/L

Spike 2: ClO_2^- at 15 g/L + ClO_3^- Spike at 100g/L + Transition Metals Spike at 0.2 mg/L

Spike 3: ClO_2^- spike at 15 g/L + Br^- at 15 g/L

Figure 3.12 shows the average concentration of perchlorate vs. time for each of the spike experiments listed above. As predicted from previous experiments, the addition of chlorite with the transition metal ions does not appear to have a synergistic effect on the formation of perchlorate, though the high chlorate/chlorite ion spike was able to increase the rate of perchlorate ion production beyond that of the control (likely due to the dependence upon chlorate ion concentration).

As a follow-up experiment, noble metals ions were spiked into sodium hypochlorite solutions as a group (Ag^+, Au^+, Ir^+, Pd^+, Pt^+) at 0.2 mg/L while iridium ion was also spiked alone into a second set of solutions at 0.2 mg/L:

Spike 4: Noble Me Ions (Ag^+, Au^+, Ir^+, Pd^+, Pt^+) at 0.2 mg/L

Spike 5: Iridium Ion (Ir^+) at 0.2 mg/L

Table 3.4 provides perchlorate ion concentration results tabulated per day, showing no effect from the presence of noble metal ions on perchlorate ion formation. These data are represented graphically in Figure 3.13, lending further evidence to the lack of involvement by the tested noble metal ions on hypochlorite decomposition and perchlorate formation. Perchlorate

ion concentration in spiked samples and control samples appears to be of the same statistical data set (i.e, as if replicate samples of the same hypochlorite ion solution), leading to the conclusion that the noble metal ions at 0.2 mg/L concentration have very little or no effect.

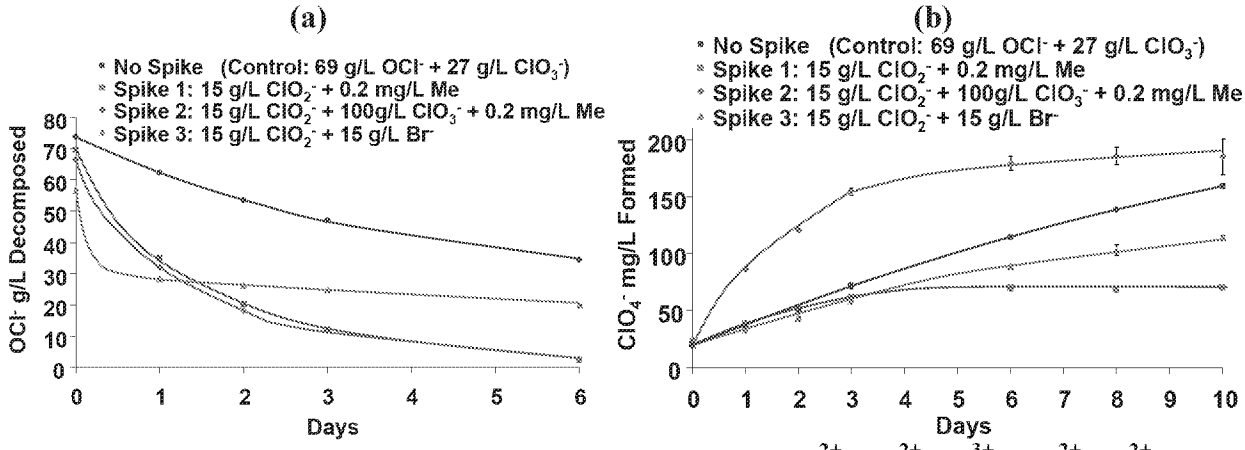


Figure 3.12 Effects of transition metals ions spikes (Me = Co^{2+}, Cu^{2+}, Fe^{3+}, Mn^{2+}, Ni^{2+}), 1.7 M hypochlorite, at 50 °C, (a) decomposition of hypochlorite; (b) formation of perchlorate

Table 3.4
Change in perchlorate concentration over the duration of incubation study 5-C with 1.7 M hypochlorite at 50 °C

Perchlorate results (mg/L)	Day						
	0	1	2	3	6	8	10
Spike 4: 0.2mg/L Noble Me	20.4	37.6	50.5	71.5	108	135	161
Spike 4: 0.2mg/L Noble Me (Duplicate)	20.7	37.1	52.0	70.9	112	137	150
Spike 5: 0.2mg/L Ir	19.7	40.3	54.0	69.5	115	128	161
Spike 5: 0.2mg/L Ir (Duplicate)	20.2	40.5	52.0	72.5	115	140	162
No spike: Control	20.0	34.6	52.0	74.4	114	138	157
No spike: Control (Duplicate)	19.9	37.8	50.0	69.4	115	139	161
Mean	**20.1**	**38.0**	**52.0**	**71.4**	**113**	**136**	**159**
Std. Dev.	**0.4**	**2.2**	**1.4**	**1.9**	**2.8**	**4.4**	**4.6**
RSD	**2.0**	**5.8**	**2.7**	**2.7**	**2.5**	**3.2**	**2.9**

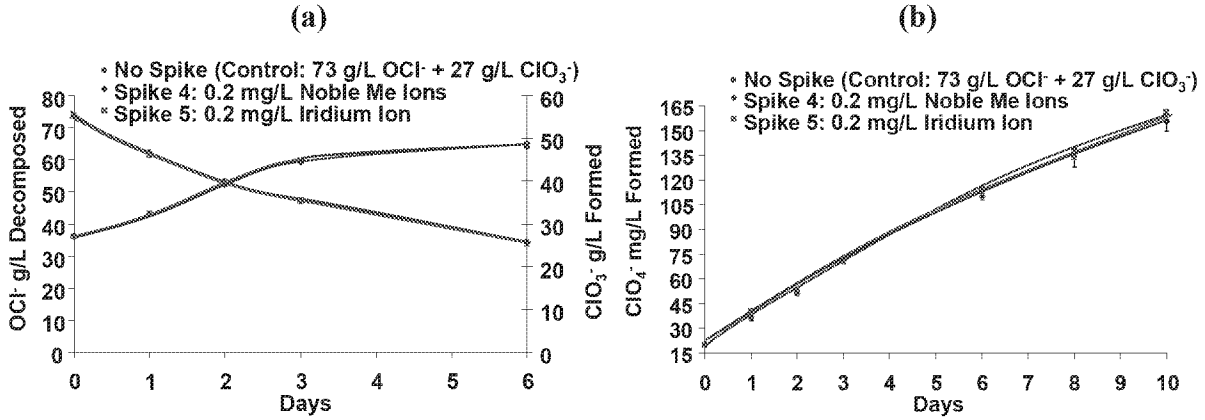


Figure 3.13 Effects of noble metals ions (Noble Me Ions =Ag^+, Au^+, Ir^+, Pd^+, Pt^+) spikes, 1.7 M hypochlorite, 50 °C (a) decomposition of hypochlorite; (b) formation of perchlorate

In summary, transition metals are unable to enhance perchlorate ion formation because they catalyze a rapid decomposition of hypochlorite ion which is needed to form perchlorate. Thus, perchlorate can theoretically be minimized under conditions which also result in a loss of hypochlorite (though this would be disadvantageous for the utility). Chlorite and transition metals do not appear to have a synergistic effect on formation of perchlorate. Hypochlorite solutions spiked with both contaminants produced perchlorate levels significantly lower than control solution. Noble metal ions spiked at 0.2 mg/L also showed little or no effect on the amount of perchlorate formed.

Bromide and Bromate Ion Effects

The effects of bromide and bromate on formation of perchlorate, bromate, and chlorate were investigated by incubating 13% bulk hypochlorite samples at 50 °C spiked with the following amounts of bromide and/or bromate, in duplicate:

Br^- Spike at 15 g/L, BrO_3^- Spike at 15 g/L, or Br^- + BrO_3^- Spike at 15 g/L

Br^- Spike at 30 g/L, BrO_3^- Spike at 30 g/L, or Br^- + BrO_3^- Spike at 30 g/L

Bromate ion concentration over time was monitored by LC-MS/MS and is shown in Figure 3.14-(a) while the change in hypochlorite ion concentration is shown in Figure 3.14 (b). Change in perchlorate ion concentration is shown in Figure 3.15.

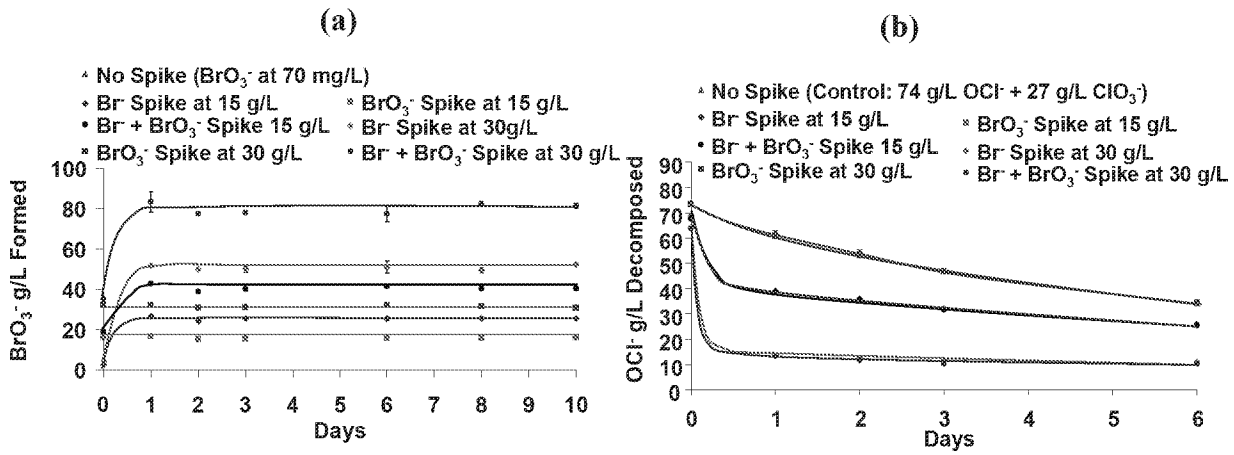


Figure 3.14: Effects of bromide and bromate, 1.7 M hypochlorite, 50 °C, (a) formation of bromate, (b) decomposition of hypochlorite

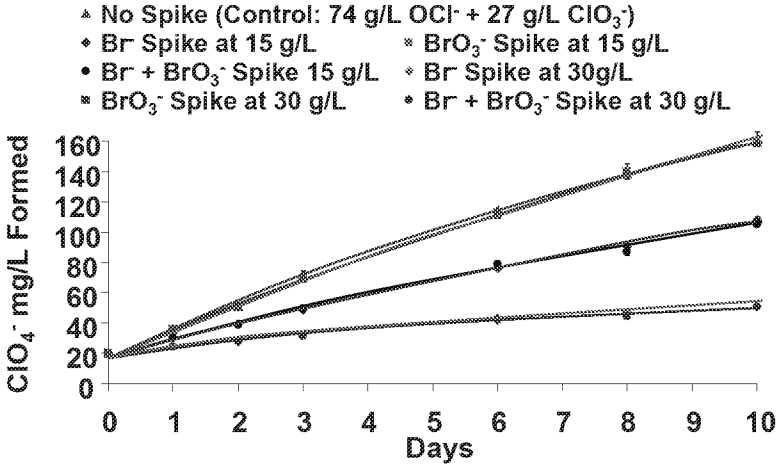


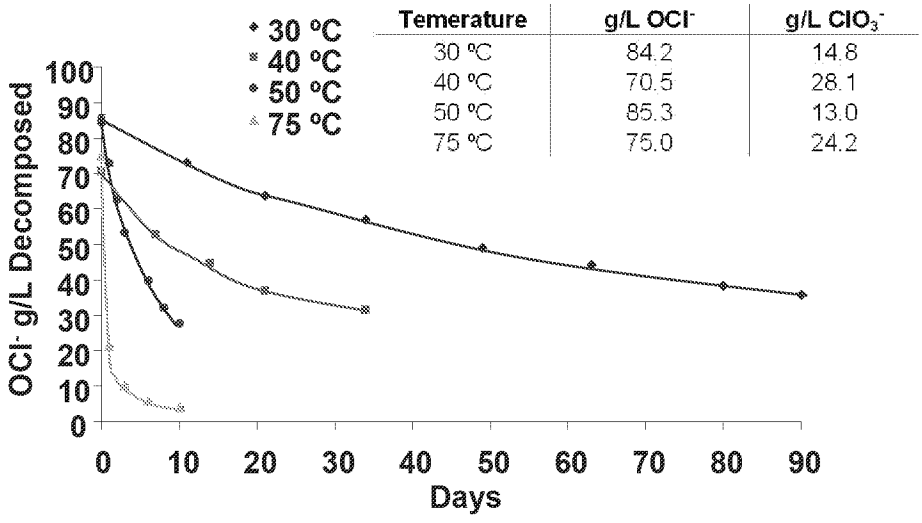
Figure 3.15 Formation of perchlorate as measured by LC-MS/MS, bromide and bromate spikes, 1.7 M hypochlorite, 50 °C

It is clear from the data that bromide ion rapidly reacts (within 1 day) with hypochlorite ion to produce bromate, hypothetically via the formation of hypobromite in a reaction mechanism similar to that of chlorate ion. The formation of perchlorate ion over time (Figure 3.15) is largely unaffected by the presence of bromate ion in solution. The presence of bromide ion did reduce the amount of perchlorate ion formed, but is likely not directly related to bromide. Instead, the reduction in the rate of perchlorate ion formation is likely due to the loss of hypochlorite ion in a reaction of bromide to produce bromate, thereby reducing the amount of hypochlorite available to produce perchlorate. The effect of the presence of bromide ion is similar to that of the transition metals ions in the sense that both types of contaminant react with available hypochlorite to produce species different than the perchlorate (e.g., transition metal

catalyze decomposition of hypochlorite to produce oxygen gas, bromide is converted to bromate), thereby reducing the available hypochlorite ion for perchlorate ion formation.

Temperature Effects

The decomposition of sodium hypochlorite solutions is strongly dependent on temperature. Both the rate of hypochlorite decomposition and the rate of chlorate formation increase with increase in temperature as observed in each of the studies listed in this Chapter (see also Figures 3.16 and 3.17) and elsewhere. The effects of temperature and ionic strength have been thoroughly investigated and a comprehensive predictive model has been developed (Adam and Gordon 1999). In this study, the effect of temperature on the formation of perchlorate ion over time was also investigated. Multiple hypochlorite solutions were incubated at temperatures ranging from 30 °C to 75 °C in order to quantify the relationship between perchlorate ion formation and temperature. Results of changes in perchlorate ion concentration from several of the studies are summarized in Figure 3.18 (hypochlorite and chlorate ion concentrations form the same experiments are summarized in Figures 3.16 and 3.17). Although the hypochlorite solutions varied in chlorate ion concentration, qualitatively one can still see that the rate of perchlorate ion formation is also strongly dependent on temperature. Thus, temperature effects were incorporated into the detailed chemical rate law discussed in Chapter 4.



Temerature	g/L OCl^-	g/L ClO_3^-
30 °C	84.2	14.8
40 °C	70.5	28.1
50 °C	85.3	13.0
75 °C	75.0	24.2

Figure 3.16 Decomposition of hypochlorite ion and formation of chlorate ion in sodium hypochlorite solutions stored at different temperature; (Initial concentrations of hypochlorite and chlorate are given in the right corner of the figure)

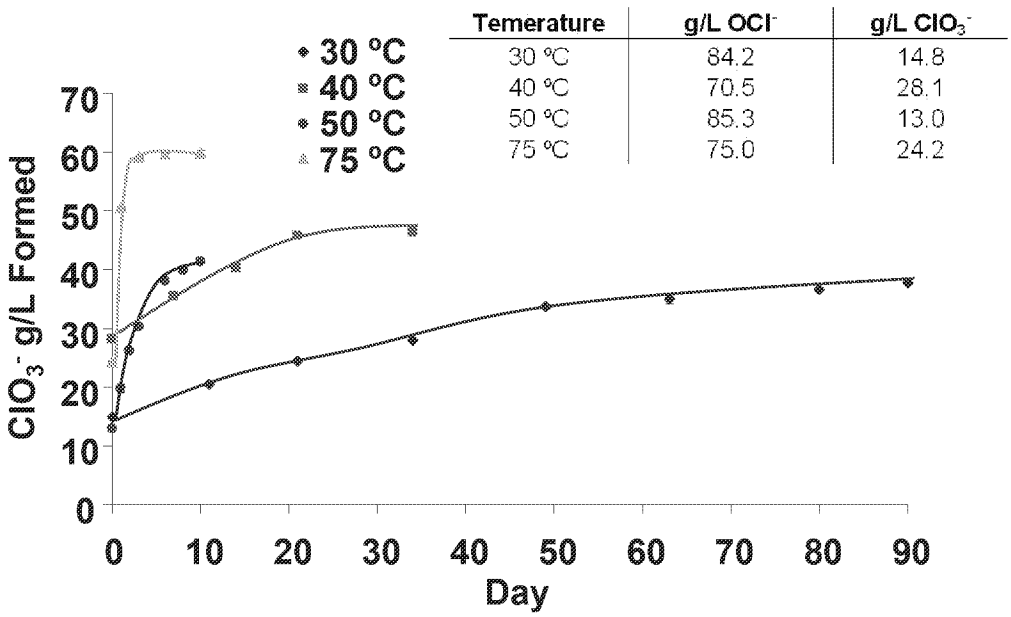


Figure 3.17 Formation of chlorate ion in sodium hypochlorite solutions stored at different temperature; (Initial concentrations of hypochlorite and chlorate are given in the right corner of the figure)

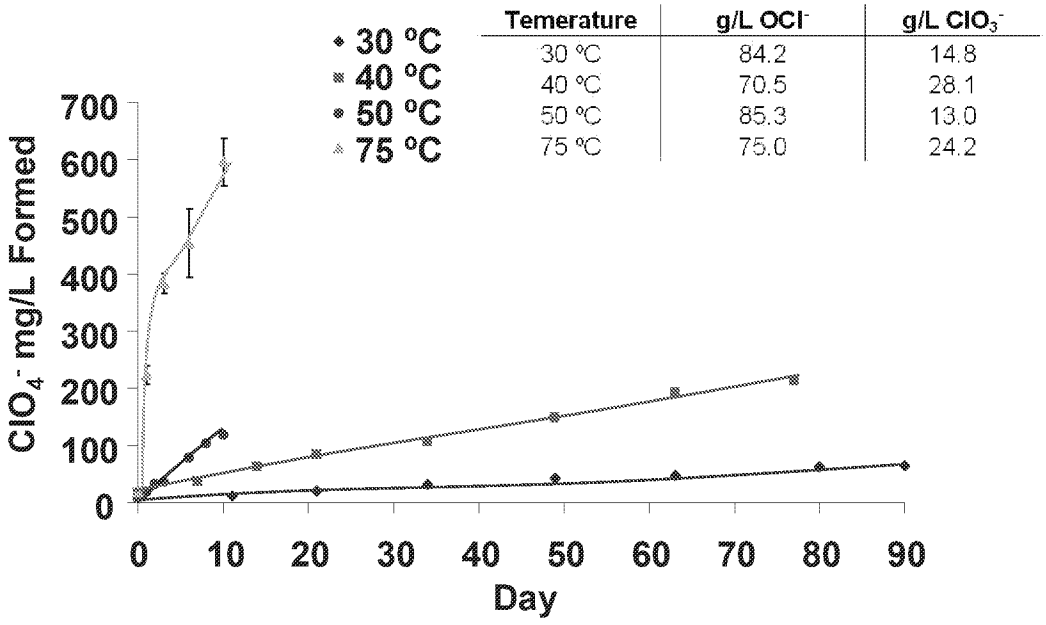


Figure 3.18 Formation of perchlorate ion in sodium hypochlorite solutions stored at different temperature; Error bars are based on difference in result of two duplicate samples; (Initial concentrations of hypochlorite and chlorate are given in the right corner of the figure)

Ionic Strength Effects

Given that higher ionic strength increases the rate of decomposition of hypochlorite ion and increases the rate of chlorate ion formation (Adam 1994; Gordon, et al. 1997; Adam and Gordon 1999), it was hypothesized that a higher ionic strength would likewise increase the rate of perchlorate ion formation. To investigate effects of ionic strength on formation of perchlorate, solutions of sodium hypochlorite were incubated at 40 °C and 60 °C with different ionic strengths achieved by dilution and/or spiking with sodium chloride. Three groups of samples were incubated at 40 °C, each having varying chloride ion concentration (used to vary ionic strength), constant hypochlorite ion concentration, and a different chlorate ion concentration for each of the three groups. Another set of solutions was incubated at 60 °C and had the same initial hypochlorite and chlorate ion concentrations but varied by sodium chloride concentration.

Figure 3.19 shows the *Bleach 2001* (Adam, Gordon, and Pierce 2001) predicted decomposition of hypochlorite ion and subsequent formation of chlorate ion when additional chloride ions are added to the solution. As expected, increasing the ionic strength by chloride ion addition increases the rates of formation of chlorate ion and disappearance of hypochlorite ion. In Figures 3.20 and 3.21, similar effects are observed on the formation of perchlorate ion with respect to ionic strength at 40 °C and 60 °C. In figure 3.21, the high ionic strength and high temperature resulted in a plateau of perchlorate ion concentration due to a rapid depletion of hypochlorite ion concentration. However, unlike in the metal ion experiments whereby a rapid loss of hypochlorite resulted in little additional perchlorate ion formation, here ionic strength increased the rate *and* the total amount of perchlorate ion produced in each solution. Similar impacts on hypochlorite ion, chlorate ion, and perchlorate ion concentrations were observed in each of the ionic strength – temperature paired experiments (data not shown).

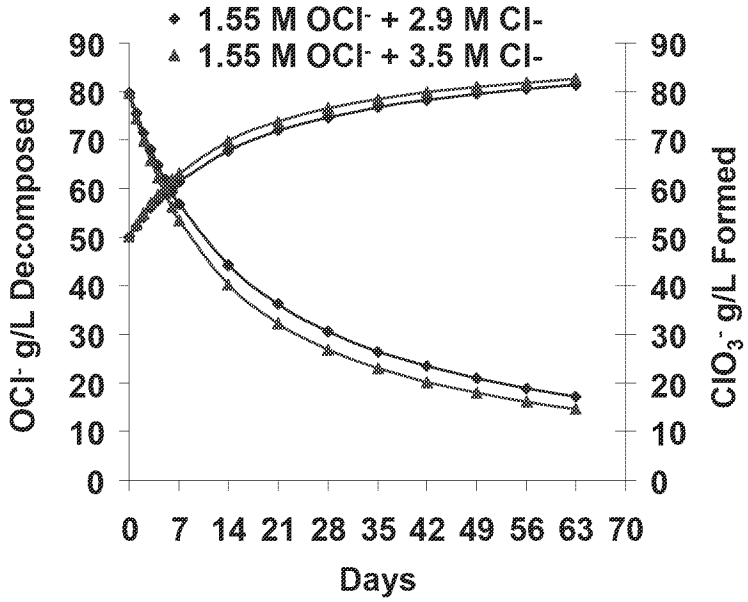


Figure 3.19 Predicted decomposition of hypochlorite ion and formation of chlorate ion in sodium hypochlorite solutions varying by concentration of chloride ion by *Bleach 2001*

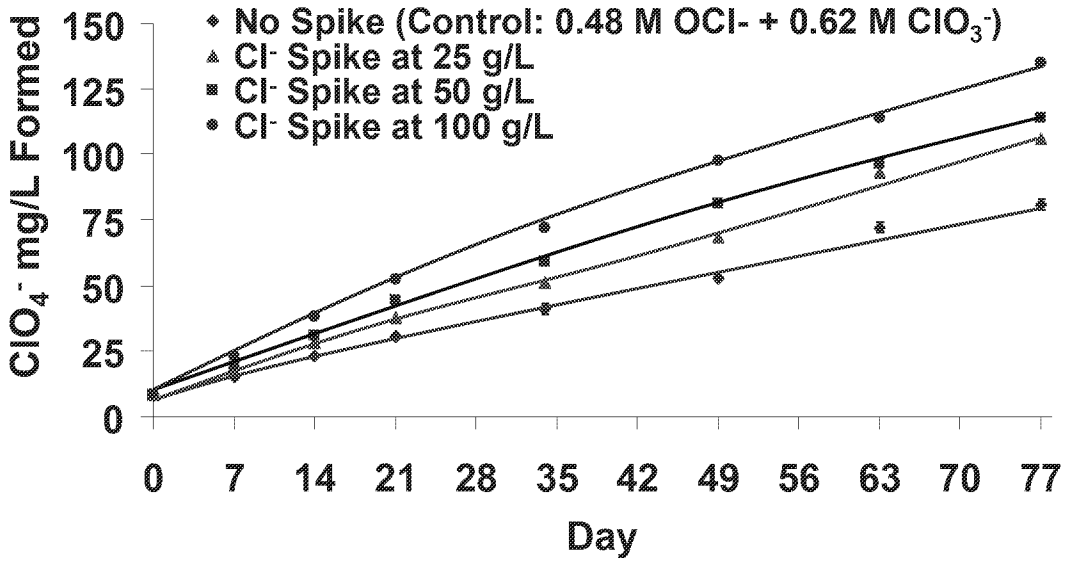


Figure 3.20 Formation of perchlorate in hypochlorite solutions spiked with variable amounts of chloride ion at 40 ºC

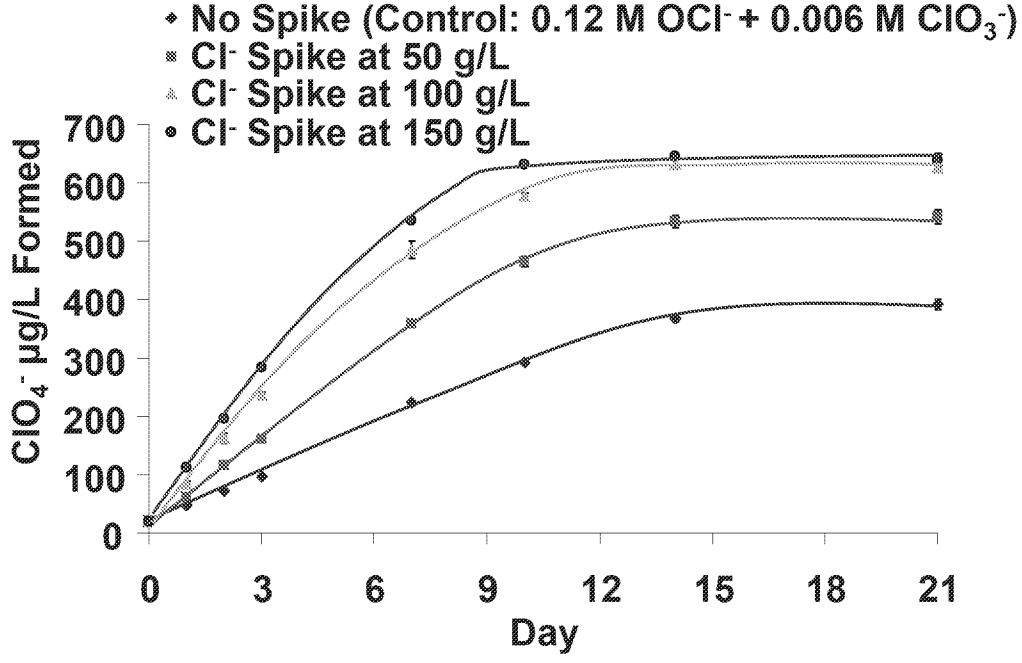


Figure 3.21 Formation of perchlorate in Hypochlorite solutions spiked with variable amounts of chloride ion at 60 ºC

Effects of pH

Sodium hypochlorite solutions are most stable in the pH 12-13 range (Adam 1994; Adam and Gordon 1999). Above pH 13, the hydroxide ion concentration exerts an ionic strength effect on the decomposition of hypochlorite ion. Below pH 11 however, an acid-catalyzed decomposition of hypochlorite ion begins to occur. At pH values lower than 10.5 this rate of decomposition continues to increase. In the pH 11 – 14 range, the decomposition of hypochlorite ion is second order in hypochlorite; in the pH 5 – 9 range, the decomposition is third order in hypochlorite. As such, there is some discontinuity that can be observed between pH of 9 and 11 in the decomposition of hypochlorite (Adam and Gordon 1999). Current guidelines recommend that sodium hypochlorite solutions should be stored in the pH 12-13 region where both the decomposition of hypochlorite ion and the formation of chlorate ion are minimized. Perchlorate ion formation, as has already been shown during the course of this report, is dependent on concentrations of hypochlorite ion, chlorate ion, and ionic strength. Thus, it is reasonable to assume that because pH affects hypochlorite ion decomposition and chlorate ion formation, pH may also affect perchlorate ion formation.

To study the pH effects on perchlorate ion formation, sodium hypochlorite solutions were prepared at three pH values (13, 11, and 9) and incubated at 40 °C. Figure 3.22 (a) shows the changes in perchlorate ion concentration over time and Figure 3.22 (b) shows the decomposition of hypochlorite ion and formation of chlorate ion of the same sodium hypochlorite solution incubated at 40 °C.

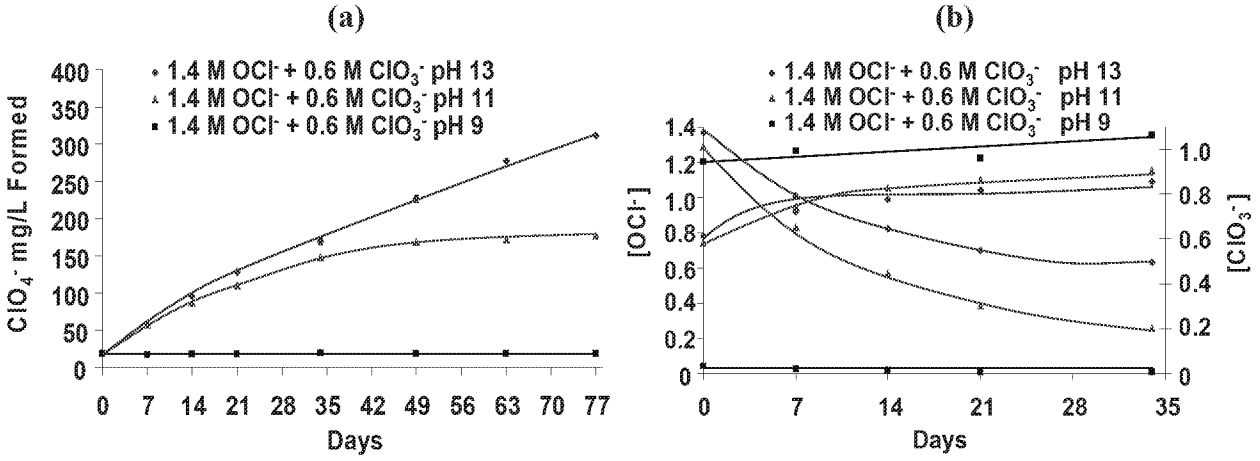


Figure 3.22 Plots of (a) perchlorate concentration vs. time; (b) hypochlorite and chlorate concentration vs. time in sodium hypochlorite solutions with initial [OCl^-] = 1.4 M and initial [ClO_3^-] =0.6 M at pH 13, 11, and 9 incubated at 40 °C

As observed in figure 3.22 (a), the increase in perchlorate ion concentration in solution adjusted to pH 9 is not appreciable above the starting concentration. However, the data presented in Figure 3.22 (b) indicate that at pH 9 the decomposition of hypochlorite ion was so rapid that by the time of analysis only trace amounts of hypochlorite ion could be detected. Thus, the effect of pH 9 during this experiment on the rate of perchlorate ion formation was inconclusive, but indicates that decreasing the pH in concentrated sodium hypochlorite solutions may affect the rate of perchlorate formation. The same conclusion was drawn from experimental data presented in Figure 3.23 (a, b). From a practical stand point, 13% NaOCl solution at pH 12.9 has a half-life of 197 days at 25 °C (*Bleach 2001* prediction), whereas the actual Hypochlorite solution adjusted to pH 9 decomposed in a matter of hours. Each of the pH-perchlorate figures presented here indicate that at pH values lower than 13 (which served as the control), there is less perchlorate ion formed. This result can be explained by the fact that at lower pH values the decomposition of hypochlorite ion and formation of chlorate ion are enhanced, leading to faster hypochlorite ion consumption and therefore less perchlorate ion formation.

To investigate more thoroughly the impact of pH in the 9 – 11 regions, a follow-up incubation study at 60 °C was conducted on OSG Hypochlorite produced at SNWA (more dilute than bulk and at a lower pH) and adjusted with NaOH to vary the pH. The stock solution (control) of sodium hypochlorite had a pH of 9.35. Aliquots of this solution were adjusted to pH =10.65, 11.90 and 13.3 by addition of sodium hydroxide and then incubated at 60 °C. As expected, the control solution at pH 9.35 had the fastest rate of hypochlorite ion decomposition, and the fastest rate of chlorate ion formation as shown in Figures 3.24 (a, b) and 3.25.

Interestingly, the rate of perchlorate ion formation was also enhanced in the sodium hypochlorite solution having an initial pH of 9.35 (Figure 3.25) though the overall perchlorate concentration at the end of the experiment was less than or the same as the other solutions tested at different pH. The hypochlorite solutions with initial pH values of 10.65 and 11.90 produced very similar amounts perchlorate ion, while solution with pH 13.30 produced more perchlorate by 21 days of incubation, and had the second fastest rate of perchlorate formation. This can be explained by the fact that the ionic strength of pH=13.30 solution was significantly higher than the rest. Table 3.5 shows ionic strength and total dissolved solids of each solution derived from specific conductance measurements.

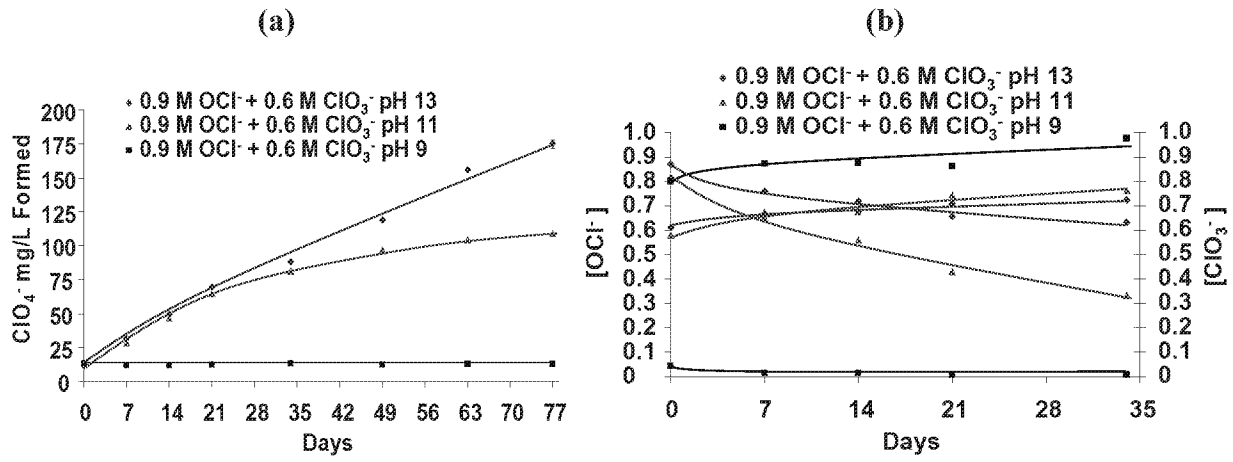


Figure 3.23 Plot of (a) perchlorate concentration vs. time in sodium; (b) hypochlorite and chlorate concentration in hypochlorite solutions with initial [OCl^-] = 0.9 M and initial [ClO_3^-] = 0.6 M at pH 13, 11, and 9, incubated at 40 °C

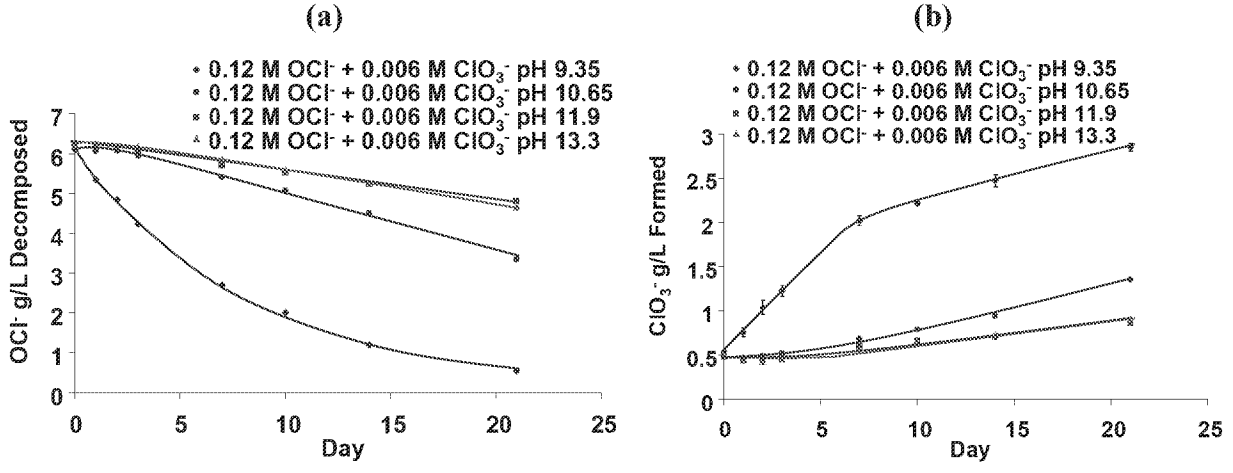


Figure 3.24 Effect of pH on hypochlorite decomposition (a) and chlorate formation (b) in OSG hypochlorite solutions at 60 °C

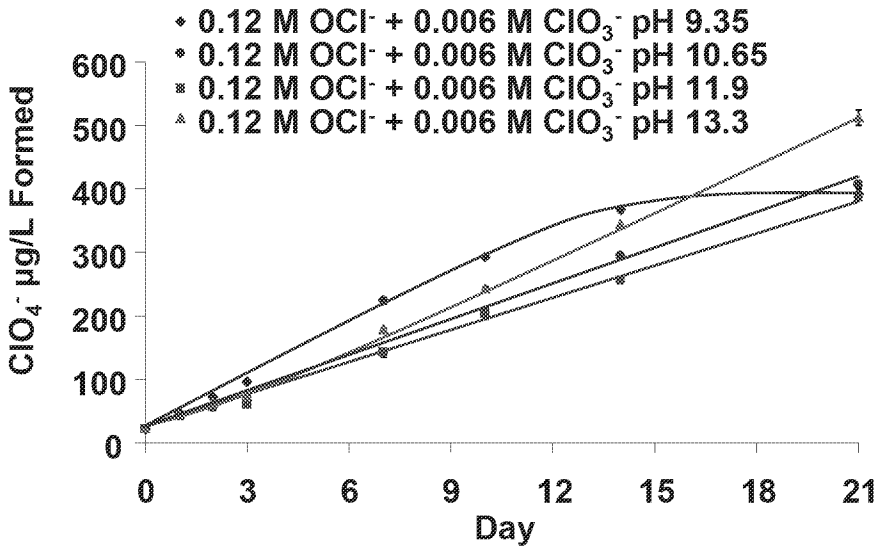


Figure 3.25 Effect of pH on perchlorate formation in OSG hypochlorite solutions at 60 °C

Enhancement of the initial rate of perchlorate ion formation at pH 9.35 suggests that there may be a pH dependence. However, over time the amount of perchlorate produced at this pH compared to higher pH is less due to the more rapid decrease in hypochlorite ion concentration at the lower pH. From a practical standpoint, the pH effect is not significant since most of bulk sodium hypochlorite solutions have a pH above 11 and OSG Hypochlorite is rarely stored for more than 24 to 48 hours. Furthermore, the impact of ionic strength observed from adjusting the pH with sodium hydroxide points towards the issue of ionic strength acting as a "master variable" (in addition to hypochlorite ion concentration and chlorate ion concentration) that out-weighs any pH effects that might be observed.

Table 3.5
Ionic strength and Total Dissolved Solids (TDS) of sodium hypochlorite solutions with initial [OCl^-]=0.120 ±0.001M (Measured by titration), [ClO_3^-]=0.006±0.0003 (measured by LC-MS/MS) with pH adjusted using NaOH

pH	[OCl^-]	[ClO_3^-]	Ionic strength, M	TDS, g/L
9.35	0.118_4	0.006_5	**0.89**	**35.6**
10.65	0.120_3	0.005_9	**0.88**	**35.2**
11.9	0.120_9	0.006_0	**0.90**	**36.1**
13.3	0.120_9	0.005_8	**2.57**	**103.0**
Mean	**0.120**	**0.006_0**		
Std. Dev.	0.001	0.000_3		
RSD	1.00	4.96		

SUMMARY

The data presented in this Chapter represent the experimental work designed to determine the factors impacting perchlorate ion formation in sodium hypochlorite solutions. The effect investigated included: concentration of hypochlorite and chlorate ions, concentration of chlorite ion, metal ion effects, bromide and bromate ion effects, temperature, ionic strength, and pH. The effects of each of these factors can be grouped into four major categories: (1) Factors directly (mechanistically) impacting the rate of perchlorate formation; (2) Factors indirectly impacting the rate of perchlorate formation by changing hypochlorite ion or chlorate ion concentrations; (3) Factors having no observable effect on perchlorate formation; and (4) Environmental factors.

1. Factors directly (mechanistically) impacting the rate of perchlorate formation

    a. Hypochlorite ion concentration: higher concentration results in a faster rate of perchlorate formation

    b. Chlorate ion concentration: higher concentration results in a faster rate of perchlorate formation

    c. Ionic strength: higher ionic strength results in a faster rate of perchlorate formation

2. Factors indirectly impacting the rate of perchlorate formation by changing hypochlorite ion or chlorate ion concentrations

    a. Metal ions, rather than catalyzing perchlorate formation, actually assist in the minimization of perchlorate ion formation at the expense of a loss of hypochlorite ion concentration in the Hypochlorite solution.

    b. The presence of bromide ion reduces the rate of perchlorate ion formation by consuming hypochlorite ion for the production of bromate ion. Thus, less hypochlorite ion is available for perchlorate ion formation.

    c. Addition of chlorite ion does not enhance the rate of perchlorate ion formation mechanistically. However, chlorite did impact the concentration of hypochlorite and chlorate ions, thereby causing an incremental increase in perchlorate ion formation.

3. Factors having no observable effect on perchlorate formation

    a. BrO_3^-, Ag(I), Au(I), Ir(I), Pt(I), and Pd(I) had no observable effect either on the perchlorate formation, hypochlorite decomposition, or chlorate formation

4. Environmental factors

    a. The impact of pH clearly changes the rate of decomposition of hypochlorite ion. While it is possible that there is a mechanistic

consideration in the formation of perchlorate ion, from a practical standpoint pH is considered an indirect, environmental factor that can be adjusted as needed.

b. Temperature clearly impacts the rate of perchlorate ion formation in addition to the rate of hypochlorite ion decomposition and chlorate ion formation. However, temperature can be adjusted/controlled to some extent, thus was considered an environmental factor

Based on the observations listed above, the controlling variables in the rate of perchlorate ion formation are concentration, ionic strength, temperature, and pH. From a practical standpoint, pH can be ruled out as a contributing factor because it is expected that only bulk hypochlorite solutions with a pH of 11 to 13 will be stored for any period of time. Thus, one environmental factor and three mechanistic factors remain. Any change in concentration of hypochlorite or chlorate strongly impacted the rate of perchlorate formation. However, the inclusion of constant molar product of hypochlorite and chlorite ions into the experimental matrix led to two possible scenarios: the order with respect to hypochlorite may be higher than one OR the rate of perchlorate formation may be dependent on another variable not considered during the initial design of the constant-molar-product experiments (e.g., ionic strength). Therefore, the determination of the rate law of perchlorate ion formation discussed in the next Chapter incorporates considerations of concentrations of hypochlorite and chlorate ions as well as accounting for environmental factors such as ionic strength and temperature.

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CHAPTER 4
FORMULATION OF INITIAL MODEL FOR PREDICTING PERCHLORATE FORMATION IN HYPOCHLORITE SOLUTIONS

APPROACH

Detailed in the summary of Chapter 3 were two sets of factors controlling the rate of perchlorate formation: mechanistic factors (i.e., chlorate ion concentration, hypochlorite ion concentration, and ionic strength) and environmental factors (i.e., temperature). The results of constant molar-product (of hypochlorite and chlorate ions) experiments showed that sample solutions containing the highest concentration of hypochlorite had a faster rate of perchlorate formation and a greater concentration of perchlorate formed. This strongly suggests that either (1) the order with respect to hypochlorite is higher than one, or (2) the rate of perchlorate formation may be dependent on an additional variable such as ionic strength. Additionally, the data presented in Chapter 3 also suggested a strong temperature dependence for the rate of perchlorate formation. Therefore, in order to elucidate the chemical rate law and develop a "Predictive Model" the following approaches were taken to eliminate possibilities and determine the variables that best correlate with perchlorate formation:

1. Determine the reaction order with respect to hypochlorite and chlorate. Initially, assume the reaction order is one in both hypochlorite and chlorate.

2. If the rate constant of the rate law based on first order in each reactant does not correlate well with concentration, then consider a higher order for one or both reactants. If the order is higher than one, then a second reaction pathway (parallel or consecutive) should be considered. Determine whether a parallel reaction pathway or consecutive reaction pathway can be fitted.

3. Determine what correlations, if any, exist between ionic strength, temperature, and rate of perchlorate formation. In this case, the assumption of first order in hypochlorite and chlorate ions is initially used to convert the rate of perchlorate formation (change in perchlorate concentration per unit time) to the observed rate of formation (k_{obs}, which is the rate of formation normalized to the molar product of hypochlorite ion and chlorate ion concentrations). Only data from experiments conducted at the same, constant temperature are compared.

4. Determine the temperature dependence of the rate of perchlorate formation by using the Eyring Equation. From this, the enthalpy and entropy can be determined and later used to correct for variations in temperature.

5. Develop a model based on the established relationship between prediction of the perchlorate formation rate constant, ionic strength, and temperature.

6. Fit the experimental data using the determined rate constant based on various reaction pathways, and determine which reaction pathway provides the best fit.

DETERMINATION OF THE RATE LAW FOR PERCHLORATE ION FORMATION

Hypochlorite and chlorate ion concentrations were found to have a strong effect on the rate of perchlorate formation. An increase in concentration of either species consistently caused an increase in the rate and final amount of perchlorate formed. Other chemical species, such as bromide, chlorite, and transition metals were identified to have a direct impact on hypochlorite and chlorate, thereby causing changes in concentrations of hypochlorite or chlorate which affected perchlorate formation. Thus, the hypothesis that the formation of the perchlorate ion was a direct result of reactions between hypochlorite and chlorate ions (Equation 3.3, Chapter 3) was assumed correct.

$$OCl^- + ClO_3^- \rightarrow ClO_4^- + Cl^- \qquad \textbf{(3.3)}$$

Given that perchlorate formation was dependent on both concentrations of hypochlorite and chlorate the following rate law was proposed:

$$Rate = \frac{d[ClO_4^-]}{dt} = k_2[OCl^-]^m \times [ClO_3^-]^p \qquad \textbf{(3.4)}$$

A series of experiments were designed to determine the reaction order with respect to hypochlorite and chlorate ions (reported in Chapter 3, Figures 3.1, 3.3). In these experiments, either OCl^- or ClO_3^- concentration was varied while holding the concentration of the other reactant constant. The observed rate of perchlorate formation was then correlated with the concentration of each reactant by taking the natural log of Equation 3.4 to yield Equation 4.1:

$$\ln(Rate) = \ln k_2 + m \ln[OCl^-] + p \ln[ClO_3^-] \qquad \textbf{(4.1)}$$

The second order rate constant (k_2) and the value of the reaction order with respect to OCl^- and ClO_3^- (m and p, respectively) are determined by least squares data fitting. The next several pages are devoted to fitting natural log of the rate of perchlorate formation versus natural log of the chlorate and hypochlorite concentrations.

Order with Respect to Chlorate Ion: $\ln(\frac{dClO_4^-}{dt})$ vs. $\ln [ClO_3^-]$

The order with respect to chlorate was determined by plotting the natural log of the rate of perchlorate formation against the natural log of the chlorate ion concentration in the experiments with constant hypochlorite ion concentration and variable chlorate ion concentration. The slope of the line represents the order with respect to chlorate (p) while the intercept is the sum of $\ln(k_2)$ and m*ln[OCl-] (Equation 4.1). Figure 4.1 (a-d) shows plots of ln(Rate) vs. $\ln[ClO_3^-]$ at different temperatures and incubation lengths. The slope and Pearson correlation coefficients (R^2) across all temperatures investigated are summarized in Table 4.1. As can be seen from Table 4.1, fitting ln[Rate] vs $\ln[ClO_3^-]$ in general produces linear correlation with an average R^2=0.9838, and average slope of 1.05 ± 0.105. This strongly suggests that the order of the reaction is first order with respect to chlorate ion.

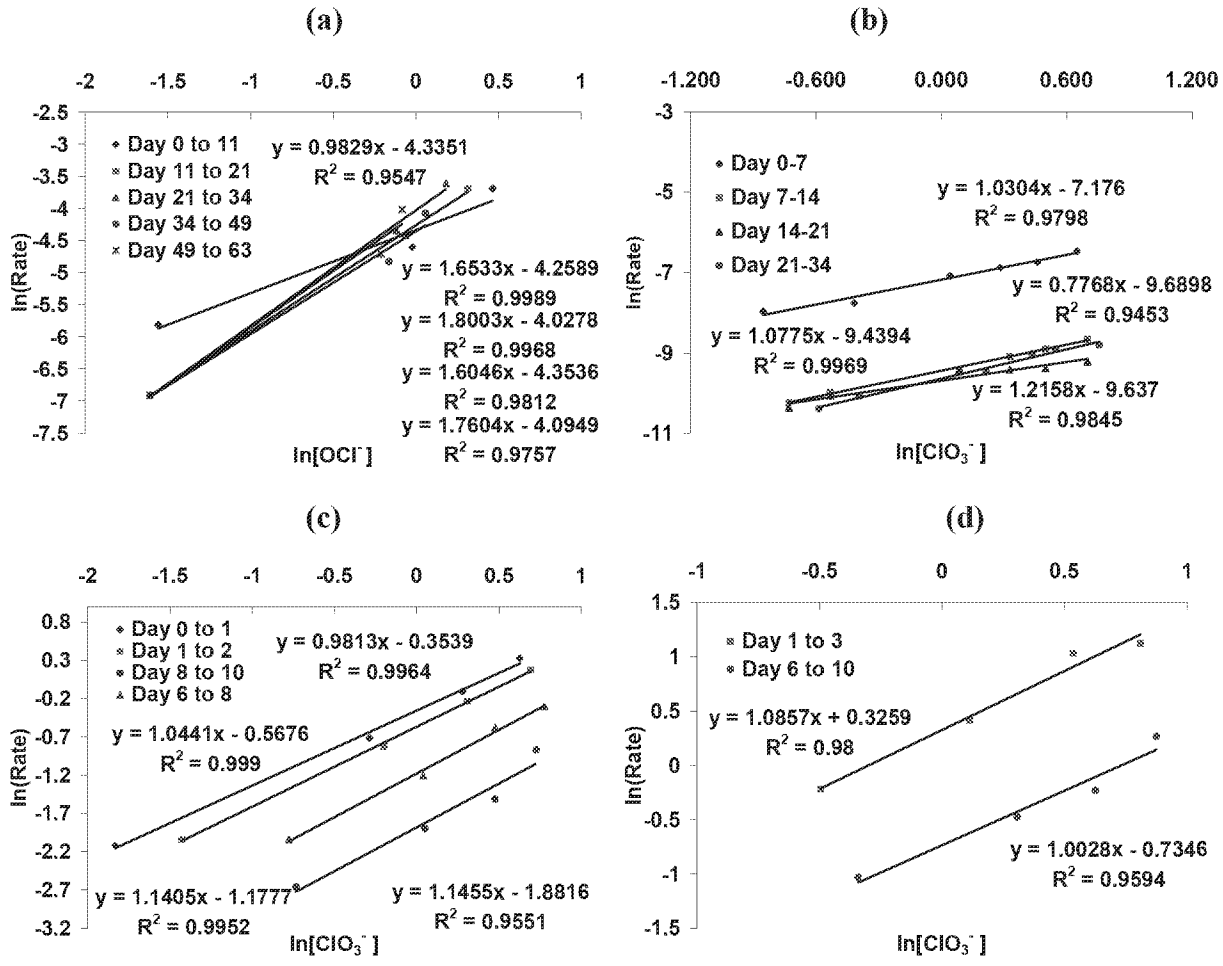

Figure 4.1 Plot of ln(Rate of perchlorate formation) vs. ln[ClO_3^-] at (a) 30 °C, (b) 40 °C, (c) 50 °C, and (d) 75 °C

Table 4.1
Slope and Pearson correlation coefficients for relationship between ln[Rate] and ln[ClO_3^-] at different temperatures

T, °C	Slope	R^2
30	1.068	0.9990
30	0.999	0.9999
30	1.031	0.9983
40	1.030	0.9798
40	1.078	0.9969
40	0.777	0.9453
40	1.216	0.9845
50	0.981	0.9964
50	1.044	0.9990
50	1.146	0.9551
50	1.141	0.9952
76	1.086	0.9800
76	1.003	0.9594
Mean	**1.05 ± 0.105**	**0.9838**

Order with Respect to Hypochlorite Ion: $\ln(\frac{dClO_4^-}{dt})$ vs. ln [ClO_3^-]

The order with respect to hypochlorite was determined by plotting ln[Rate] vs ln[OCl^-] in the set of experiments with constant chlorate ion concentration and variable hypochlorite ion concentration. The slope of the line should represent the order with respect to hypochlorite (*m*) while the intercept is the sum of ln(k_2) and p*ln[ClO_3^-] (Equation 4.1). Figure 4.2 (a-d) shows plots of ln(Rate) vs. ln[OCl^-] at different temperatures and incubation periods. It is immediately evident from the data that the slope varies within individual experiments as well as by temperature and by time. Thus, either the order with respect to hypochlorite is greater than one or another variable is controlling the reaction rate.

Given the disagreement within the data regarding the order with respect to hypochlorite, two explanations were possible: (1) The order with respect to hypochlorite is greater than one due to second reaction pathway or (2) Another variable such as ionic strength was also impacting the rate of perchlorate formation. Thus, while new data (and data already collected) were incorporated into hypothetical considerations of higher order models in hypochlorite (with parallel or consecutive reaction pathways), additional experiments were designed to investigate the effects of ionic strength on perchlorate formation.

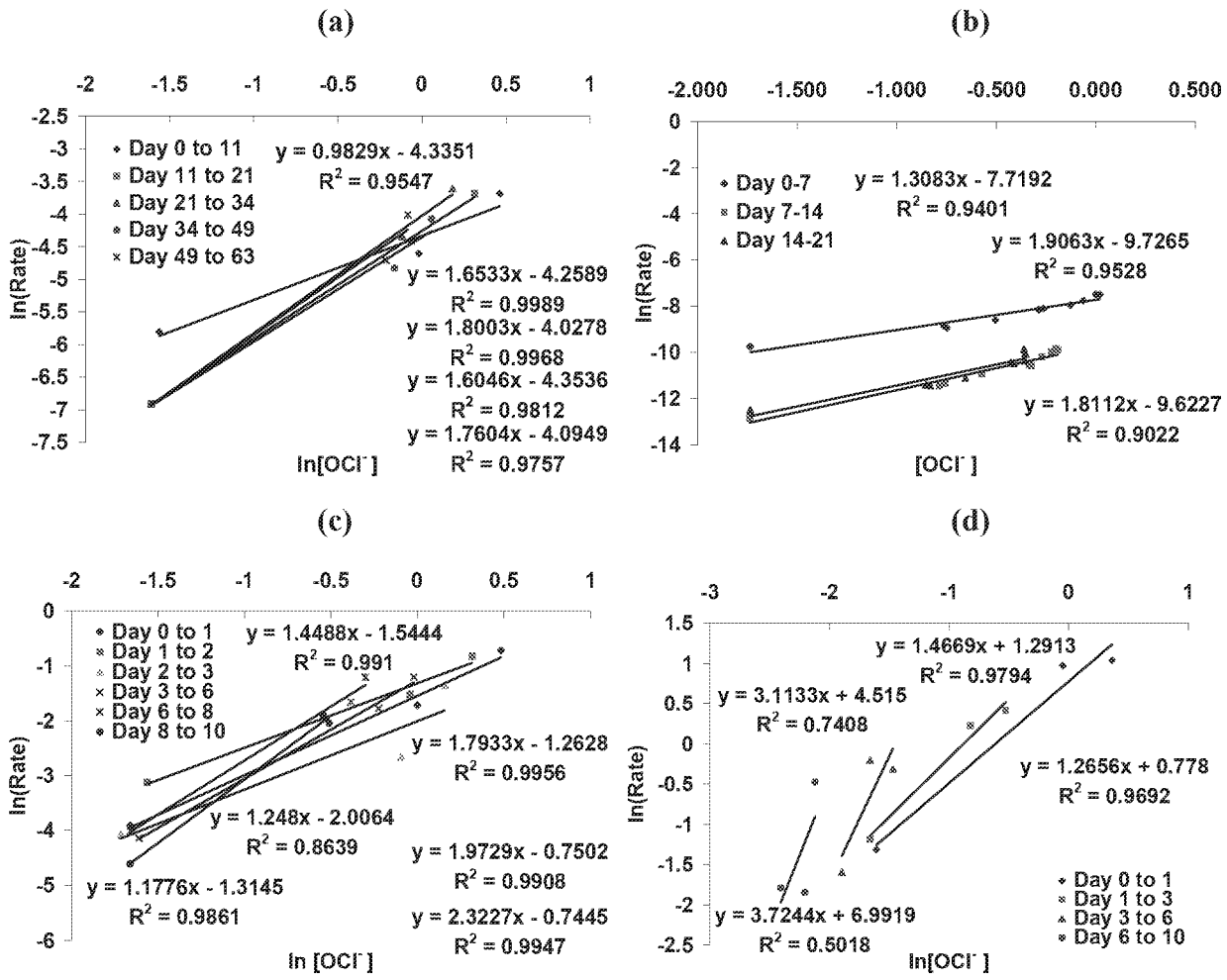

Figure 4.2 Plots of ln(Rate of perchlorate formation) vs. ln [OCl^-] at: (a) 30 °C , (b) 40 °C, (c) 50 °C, and (d) 75 °C

Reaction Order Greater than One with Respect to Hypochlorite: Parallel or Consecutive Reaction Pathways

The variability in the order with respect to hypochlorite, suggested that the order of the perchlorate formation is higher than first order in hypochlorite ion. By taking only the initial rate of perchlorate formation from constant-chlorate-variable-hypochlorite experiments conducted at 75 °C, 50 °C, 40 °C, and 30 °C and plotting that against the log of the hypochlorite ion concentration, the slope of the line is suggestive of a reaction order of 1.6 in hypochlorite (Figure 4.3-a) and 1.0 in chlorate (Figure 4.3-b). Such an empirically-derived rate law is summarized in Equation 4.2 but does not contain any explanation of species involved in perchlorate formation nor does it take into consideration the significant contribution of ionic strength in chlorate formation (Adam and Gordon 1999) or perchlorate formation (Chapter 3).

$$Rate = \frac{d[ClO_4^-]}{dt} = k_{obs}[OCl^-]^{1.6}[ClO_3^-]^1 \qquad \textbf{(4.2)}$$

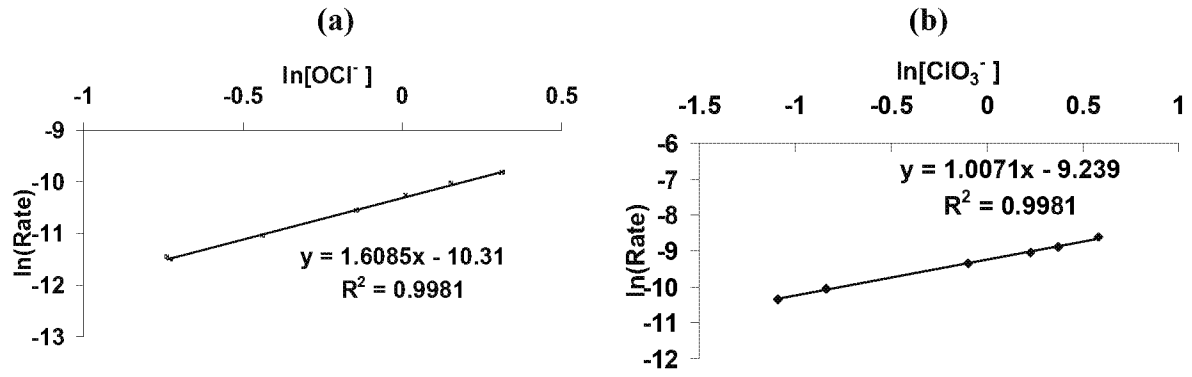

Figure 4.3 Plot of Rate vs ln [OCl^-] (a) and ln[ClO_3^-] (b)

To elucidate the order with respect to hypochlorite further, and to provide more of a mechanistic explanation of the rate of formation, one area explored was the possibility of a second reaction that is second order in hypochlorite. In a parallel reaction, one pathway could be first order in hypochlorite while a second reaction could be second order in hypochlorite. In a consecutive reaction, the order with respect to hypochlorite could be second order, followed by a first order reaction (or vice versa). The hypothetical rate law equations are shown in Equation 4.3 for the parallel reaction mechanism and Equation 4.4 for the consecutive reaction mechanism.

$$Rate = \frac{dClO_4^-}{dt} = k_1[OCl^-]^1[ClO_3^-]^1 + k_2[OCl^-]^2[ClO_3^-]^1 \qquad \textbf{(4.3)}$$

$$Rate = \frac{dClO_4^-}{dt} = \frac{k_a[OCl^-]^2[ClO_3^-]^1}{1 + k_b[OCl^-]^1} \qquad \textbf{(4.4)}$$

Parallel Reactions

In the investigation of a parallel reaction pathway, data from experiments that varied in concentration of hypochlorite but were constant in chlorate can be used to determine the values of k_1 and k_2. First, Equation 4.3 was rearranged by dividing by the molar product of hypochlorite and chlorate to yield Equation 4.5.

$$\frac{Rate}{[OCl^-]^1[ClO_3^-]^1} = k_1 + k_2[OCl^-]^1 \qquad \textbf{(4.5)}$$

By using Equation 4.4, when [Rate/([OCl^-][ClO_3^-])] is plotted vs. [OCl^-], a linear correlation will provide values of k_2 (the slope of the line) and k_1 (the intercept). Example data from the 40 °C

experiment are shown in Figure 4.4. The data shown indicate a reasonable correlation (R^2 = 0.98), but the rate law still does not account for ionic strength effects.

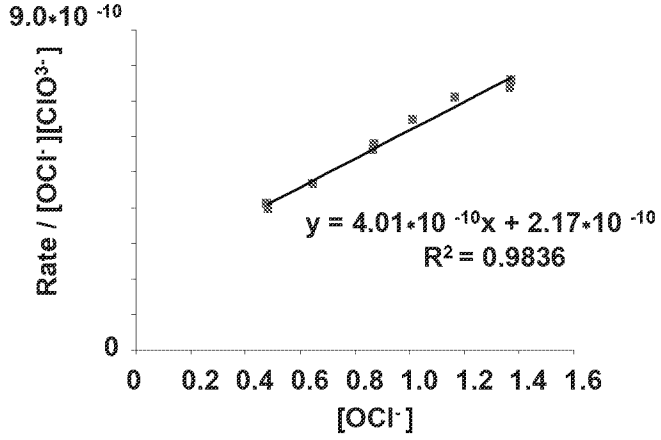

Figure 4.4 Plot of Rate/([OCl^-][ClO_3^-]) vs. [OCl^-] at 40 °C

Consecutive Reactions

In a consecutive reaction pathway, data from experiments that varied in concentration of hypochlorite but were constant in chlorate can also be used to determine the values of k_a and k_b. First, Equation 4.4 was rearranged to isolate hypochlorite, yielding Equation 4.6.

$$\frac{[OCl^-][ClO_3^-]}{Rate} = \frac{1}{k_a[OCl^-]} + \frac{k_b}{k_a} \qquad \textbf{(4.6)}$$

Thus, if ([OCl^-][ClO_3^-])/Rate is plotted against 1/[OCl^-], and the correlation is linear, the slope of the line is $1/k_a$ and the intercept is the product of k_a and k_b. Example data from the 40 °C experiment are shown in Figure 4.5. Again, a reasonable correlation of the data exists (R^2 = 0.98), though it is unclear whether this mechanism fully explains the rate of perchlorate formation, either.

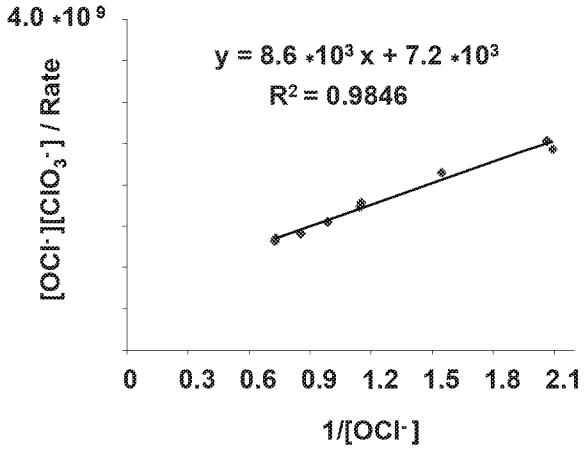

Figure 4.5 Plot of ([OCl⁻][ClO₃⁻])/Rate vs. 1/[OCl⁻] at 40 °C

Ionic Strength Effect on the Observed Rate Constant

While the discussion points mentioned in the previous sections indicate the possibility of the order with respect to hypochlorite being greater than one and that either parallel or consecutive reaction pathways could be used to explain the formation of perchlorate, a simpler explanation could involve the incorporation of ionic strength into a first order reaction in both hypochlorite and chlorate (second order overall). Similar to the parallel and consecutive reaction pathways, ionic strength correlates reasonably well to the rate of perchlorate formation (Figure 4.6). With ionic strength as the simplest explanation for the deviation in observed reaction order, a measure of the variability of ionic strength across experiments was required to further quantify the relationship. Thus, an *a posteriori* measurement of ionic strength for each incubation study sample was made by taking measurements of conductivity and converting them to ionic strength by Equation 2.12. The data are compiled in Table 4.2 for the constant chlorate concentration experiments and Table 4.3 for the constant hypochlorite concentration experiments.

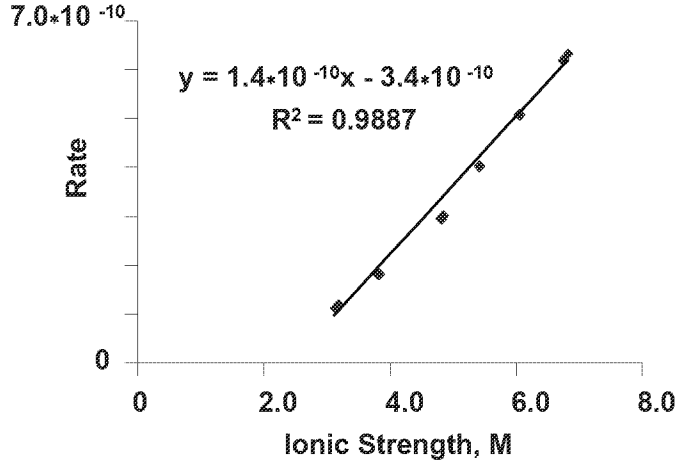

Figure 4.6 Plot of Rate of perchlorate formation vs. ionic strength at 40 °C

Table 4.2
Variation in ionic strength of sodium hypochlorite solutions during the constant [ClO_3^-] experiment at 40 °C

[OCl-] (M)	[ClO3-] (M)	Ionic strength (M)	pH
1.366	0.619	6.72	13.00
1.371	0.610	6.80	12.99
1.166	0.619	6.02	12.96
1.012	0.623	5.38	12.91
0.871	0.605	4.80	12.84
0.867	0.615	4.78	12.82
0.646	0.618	3.78	12.70
0.478	0.621	3.14	12.60
0.485	0.614	3.10	12.56
0.178	0.610	1.76	12.21
Mean	**0.615**	**4.63**	**12.76**
Std. Dev.	0.005	1.59	0.24
RSD	0.86	34.2	1.85

Table 4.3
Variation in ionic strength of sodium hypochlorite solutions during the constant [ClO_3^-] experiment at 40 °C

[ClO3-] (M)	[OCl-] (M)	Ionic strength (M)	pH
1.788	1.355	7.96	12.99
1.449	1.384	7.66	12.52
1.254	1.395	7.48	12.96
0.907	1.393	7.11	12.95
0.432	1.372	6.56	12.93
0.337	1.370	6.46	12.94
Mean	**1.378**	**7.21**	**12.88**
Std. Dev.	0.014	0.55	0.16
RSD	1.02	7.64	1.26

The variability in ionic strength in the constant chlorate data set (Table 4.2) was at least 3 times higher than that in the constant hypochlorite data set (Table 4.3). These data are easily explained by the fact that the constant chlorate experiments required significant dilution of the hypochlorite solutions while the constant hypochlorite experiments only required addition of sodium chlorate. Thus, the observed variation in the sample matrix set designed to elucidate the order of the perchlorate formation reaction was irrefutably comprised of dissimilar sample matrices. As, such the ionic strength effect must be accounted for before further consideration of higher order reaction pathway.

The first step in quantifying the relationship between ionic strength and the rate of perchlorate formation was to relate the observed rate constant at a given ionic strength to a calculated rate constant at "infinite dilution" or "zero ionic strength" (k_0). The Extended Debye-Hückel Equation, also known as the Davies Equation, can be used to relate the observed rate constant (k_{obs}) to the ionic strength of the solution by Equation 4.7. This equation is also useful for relating rate constants between experiments with different ionic strength as one can determine the theoretical rate constant at "infinite dilution" (k_0 at zero ionic strength).

$$\log(k_{obs}) = 1.02 Z_M Z_N \left(\frac{I^{0.5}}{1 + I^{0.5}} - \beta I \right) + \log(k_0) \qquad \textbf{(4.7)}$$

where,

k_{obs}	=	observed rate constant
k_0	=	rate constant at infinite dilution (zero ionic strength)
Z_M, Z_N	=	charges of individual reactants in rate determining step
β	=	experimentally determined coefficient
I	=	ionic strength (mol/L)

Since the product of $Z_M x Z_N$ = (-1 charge of OCl^-) x (-1 charge of ClO_3^-) = +1, Equation 4.7 becomes Equation 4.8:

$$\log(k_{obs}) = 1.02 \left(\frac{I^{0.5}}{1 + I^{0.5}} - \beta I \right) + \log(k_0) \qquad \textbf{(4.8)}$$

To simplify Equation 4.7 further, an assumption similar to one employed by Adam and Gordon (1999) in the determination of the relationship between the rate constant of hypochlorite decomposition and ionic strength was used: Equations 4.7 and 4.8 contain a "1.02 ($I^{1/2}$ / (1 + $I^{1/2}$)" term that is dominant at low ionic strength, and a 1.02 βI term that dominates at high ionic strength. If both terms are plotted as a function of ionic strength (Figure 4.7), it is evident that the "1.02 ($I^{1/2}$ / (1 + $I^{1/2}$)" term does not change as rapidly as the 1.02 βI term at ionic strength above 1M. Thus, this additional term could be removed from the equations to simplify when working above 1M. Since the majority of experiments performed during this project had an ionic strength in 1-7 M range, this simplification was used. Thus, Equation 4.8 can be further simplified to Equation 4.9.

$$\log(k_{obs}) = 1.02\beta I + \log(k_0) \qquad \textbf{(4.9)}$$

where $\log(k_0)$ is determined experimentally by fitting log (k_{obs}) vs I.

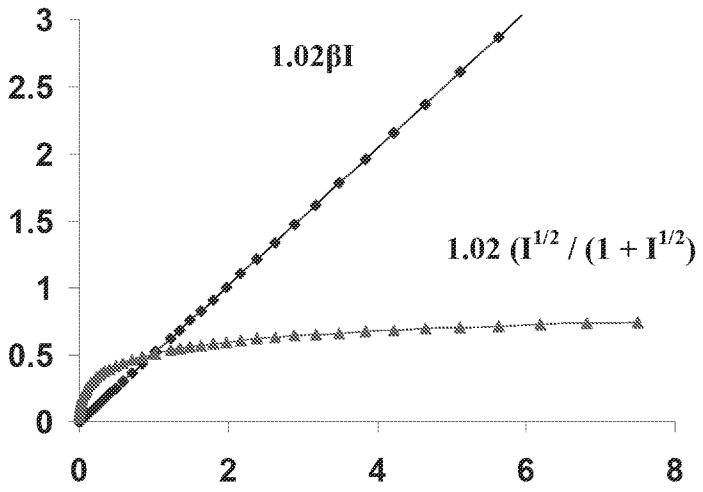

Figure 4.7 Plot of low ionic strength term [1.02 ($I^{1/2}$ / (1 + $I^{1/2}$)] and high ionic strength term [1.02 βI] as a function of ionic strength. The contribution of [1.02 βI] term becomes dominant at high ionic strength. *Assuming coefficient β value of 0.5 as an approximation.

In choosing to explore the ionic strength effect on the rate of perchlorate formation, the decision was made to use the assumption that the reaction was first order in hypochlorite and first order in chlorate in order to calculate an observed rate constant (Equation 4.10). Data from the previous incubation studies were compiled together with the ionic strength measurements and the rate of perchlorate formation was converted to the observed rate constant by dividing the average rate of initial perchlorate ion formation by the initial concentrations of hypochlorite and chlorate ions (Equation 4.10).

$$k_{obs} = \frac{\text{Rate}}{[OCl^-] \times [ClO_3^-]} \qquad \textbf{(4.10)}$$

Figure 4.8 shows the experimentally determined relationship between the rate constant and ionic strength at different temperatures. The dependence of rate constant on ionic strength increases with temperature as can be seen by increase in the slopes of the fitted lines. The slopes of the fitted lines are equal to 1.02βI and the intercepts are equal to log k_0. A summary is given in Table 4.4. The agreement of the slopes of the line between temperatures (6.35% RSD) indicate that (1) ionic strength correlates well with the rate of perchlorate formation and (2) the assumption of first order in both chlorate and hypochlorite is appropriate. Thus, ionic strength and the concentration of chlorate and hypochlorite ions were both incorporated as controlling variables in the rate of perchlorate formation.

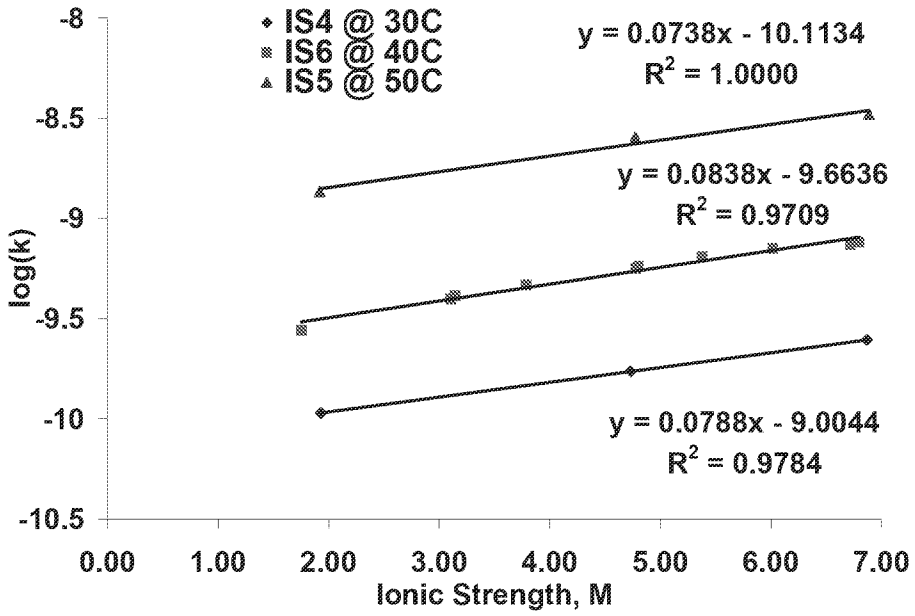

Figure 4.8 Plot of log[k_{obs}] vs. ionic strength of solution

Table 4.4
Slopes and intercept of log k_{obs} vs ionic strength-fitted lines at T = 30 °C, 40 °C, 50 °C.

Temperature (°C)	Slope	Intercept (log k_0)	k_0 in $M^{-1}s^{-1}$ (x 10^{-12})
30	0.0738	-10.1	77.0
40	0.0838	-9.66	217
50	0.0788	-9.00	990
Mean	**0.0788**		
Std. Dev.	0.005		
RSD	6.35		

Quantitation of Temperature Effects on the Rate of Perchlorate Formation

In order to combine the dependence of the observed rate constant on ionic strength and temperature, the zero ionic strength rate constant at infinite dilution (k_0) must be related to temperature dependence. Both the Arrhenius and the Eyring equations can be used to describe the temperature dependence of a reaction rate. The Arrhenius equation is applied to the kinetics of gas reactions whereas the Eyring equation (Equation 4.11), which is based on Transition State Theory, can be used for studying kinetics of reactions occurring in liquids.

$$k_0 = \frac{k_b}{h} \times T \times e^{\frac{\Delta S}{R}} \times e^{-\frac{\Delta H}{RT}} \qquad \textbf{(4.11)}$$

k_0	=	calculated from Equation 4.4	
k_b	=	Boltzmann's constant	1.381×10^{-23} J · K^{-1}
h	=	Plank's constant	6.626×10^{-34} J · s
R	=	Gas constant	8.3145 J/mol K
ΔS	=	Entropy of activation	
ΔH	=	Enthalpy of activation	

Taking the log of Equation 4.11 gives:

$$\ln\left(\frac{k_0}{T}\right) = \ln\left(\frac{k_b}{h}\right) + \frac{\Delta S}{R} - \frac{\Delta H}{RT} \qquad \textbf{(4.12)}$$

A plot of $\ln(k_0/T)$ should be a linear function of 1/T, if the data follows Equation 4.12. The slope of the line can be used to calculate ΔH and intercept can be used to calculate ΔS. Figure 4.9 shows a plot of experimentally determined $\ln(k_o/T)$ vs 1/T. Based on three points the R^2 of the line is 0.9832.

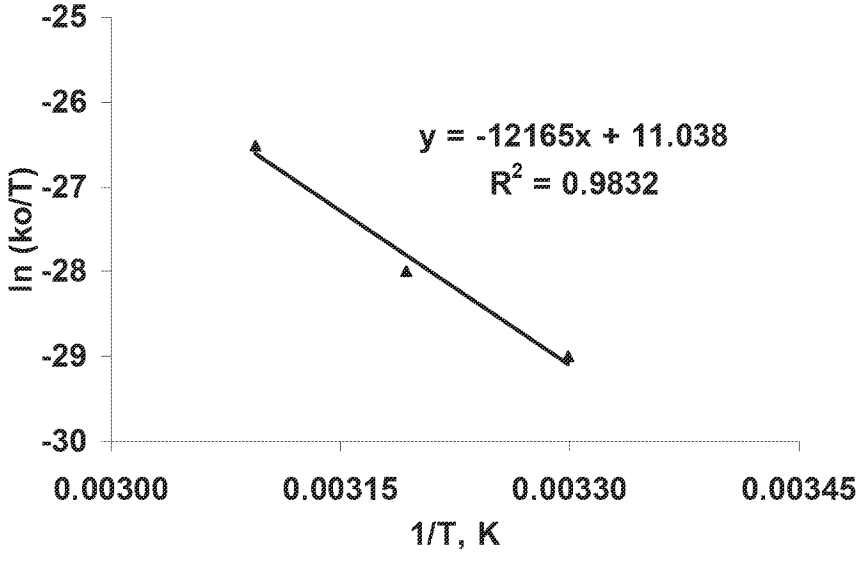

Figure 4.9 Plot of $\ln(k_o/T)$ vs 1/T for commercial hypochlorite solutions

The low Pearson correlation coefficient of 0.983 may indicate that more temperatures need to be studied and/or perhaps some temperature data points need to be repeated in order to reduce the error in the least squares estimation. However, based on the low variation observed in the fitted slopes of 6.4%, shown in Table 4.4 the Pearson correlation coefficient of 0.9832 was deemed satisfactory. The slope of the line equals $\Delta H / R$, where the intercept equals to $\ln(k_b/T) + \Delta S/R$, based on Equation 4.12. Thus, the values of thermodynamic activation parameters for the formation of perchlorate in commercial OCl^- at infinite dilution are $\Delta H = 101$ kJ/mol and $\Delta S = -106$ J/mol · K.

It should be noted that, while the temperature dependence of the reaction is expected to be linear down to zero °C, any interpretation of the model at temperatures below 30 °C (the lowest temperature at which the model was validated) should be limited to qualitative trends only until a time when the model can be validated at lower temperatures. Typically, in order to evaluate the accuracy of a model, a minimum of 1.5 half-lives is required. At temperatures below 30 °C, such validation was not possible given the allotted 11-month time frame of the project.

The Detailed Chemical Rate Law for Perchlorate Formation

Considering the data and results presented in the preceding sections of this Chapter there are three important findings: (1) The observed rate of perchlorate formation is dependent upon the concentration of hypochlorite and chlorate ions and the ionic strength. (2) The observed rate constant (k_{obs}) for perchlorate formation at the temperatures used in the incubation studies is related to ionic strength by a factor of 0.0788 M^{-1} (±0.005 M^{-1} or 6.35%). (3) The rate of perchlorate formation is temperature dependent. A generalized temperature *term* (relating zero ionic strength rate constant to temperature) can be derived from Equation 4.11 by incorporating the known values for ΔH and ΔS (Equation 4.13).

$$k_0 = 2.084\times10^{10}\times T\times e^{\frac{-1.01\times10^5}{RT}}\times e^{\frac{-106}{R}} \qquad \textbf{(4.13)}$$

Thus, substituting a factor of 0.0788 (Table 4.4) for the $1.02\beta I$ term in Equation 4.9 and the demonstrated temperature dependence (Equation 4.13) for the k_0 term in Equation 4.9 yields a quantitative chemical rate law ("Predictive Model") that can be used to calculate the predicted rate constant (k_{calc}) of perchlorate formation at any temperature and ionic strength (Equation 4.14).

$$\log(k_{calc}) = 0.0788(I) + \log\left(2.084\times10^{10}\times T\times e^{\frac{-1.01\times10^5}{RT}}\times e^{\frac{-106}{R}}\right) \qquad \textbf{(4.14)}$$

Thus, the predicted *rate* of perchlorate formation for any stepwise change in hypochlorite and chlorate ion concentrations can be calculated by a rearrangement of Equation 4.10 to yield Equation 4.15. By proxy, the concentration of perchlorate can also be calculated at any time point *provided the concentration of hypochlorite ion and chlorate ion can be predicted using Bleach 2001.*

$$Rate = \frac{dClO_4^-}{dt} = k_{calc} \times [OCl^-]^1 \times [ClO_3^-]^1 \quad \textbf{(4.15)}$$

Using the "Predictive Model" shown in Equation 4.14, calculated rate constants (k_{calc}) for perchlorate formation at specific ionic strength and temperatures were compared to experimentally observed rate constants (k_{obs}) and are summarized in Table 4.5. The percent error was calculated by taking the difference between k_{calc} and k_{obs}, then dividing the difference by k_{obs} and multiplying by 100%. The average variability between observed and predicted rate constants is less than 20% across three temperatures (30 ºC, 40 ºC, and 50ºC) and with ionic strength ranging from 1.8 mol/L to 6.9 mol/L.

Table 4.5
Calculated rate constants vs. observed rate constants at variable ionic strength and temperature

T (ºC)	I (M)	k_{obs} (M^{-1} d^{-1} x 10^6)	k_{calc} (M^{-1} d^{-1} x 10^6)	Percent Error	Average % Error	R^2 (log k vs. I)
30	6.87	21.38	21.76	1.8		
30	4.73	14.88	14.76	0.8		
30	1.93	9.24	8.88	3.8	**2.1**	***1.000**
40	6.72	63.70	78.65	23.5		
40	6.80	65.51	79.82	21.9		
40	6.02	61.29	69.24	13.0		
40	5.38	55.85	61.67	10.4		
40	4.80	49.99	55.55	11.1		
40	4.78	48.59	55.35	13.9		
40	3.78	40.26	46.19	14.7		
40	3.14	35.52	41.11	15.7		
40	3.10	34.19	40.81	19.4		
40	1.76	23.87	31.96	33.9	**18**	**0.9709**
50	6.89	285.56	277.98	2.7		
50	4.77	219.79	189.46	13.8		
50	1.92	117.24	112.84	3.8	**6.7**	**0.9784**

*R^2 of 1.000 is based on 3 data points only

The agreement between the predicted experimentally determined values, given in Table 4.5, suggests that in fact the determined relationship of the rate constant on ionic strength and temperature given by Equation 4.14 can sufficiently predict the rate constants of perchlorate formation in bulk sodium hypochlorite solutions that have pH 11-13 and ionic strength of 1-7 Molar. Thus, fitting the data using more complex reaction pathways, such as a parallel or consecutive reaction pathway is simply not applicable or practical.

VALIDATION OF THE "PREDICTIVE MODEL"

To further validate the "Predictive Model", Equation 4.14 was used to generate the rate constants needed to calculate the rate of perchlorate formation at different temperatures for several sets of samples that varied in ionic strength. The samples chosen for validation of the "Predictive Model" were bulk hypochlorite solutions used during the various incubation studies. First, *Bleach 2001* (Adam, Gordon, and Pierce 2001) was used to predict the decomposition of hypochlorite and formation of chlorate for each sample. Second, experimentally measured ionic strength, via a conductivity extrapolation, was applied to Equation 4.14 to generate rate constants of perchlorate formation at specific temperatures. Third, the obtained rate constants and the *Bleach 2001* predictions were used to predict perchlorate concentration at multiple time points during the incubation period.

Figures 4.10 and 4.11 show plots of observed and predicted (*Bleach 2001*) decomposition of hypochlorite and formation of chlorate at 30 °C and 40 °C. Figures 4.12 and 4.13 show the measured perchlorate concentrations and those calculated from the "Predictive Model". The predicted concentrations were fitted to a smoothed line, and a fixed 10% error bars were added. The error bars on all figures, unless otherwise stated, are set at a fixed value of 10%.

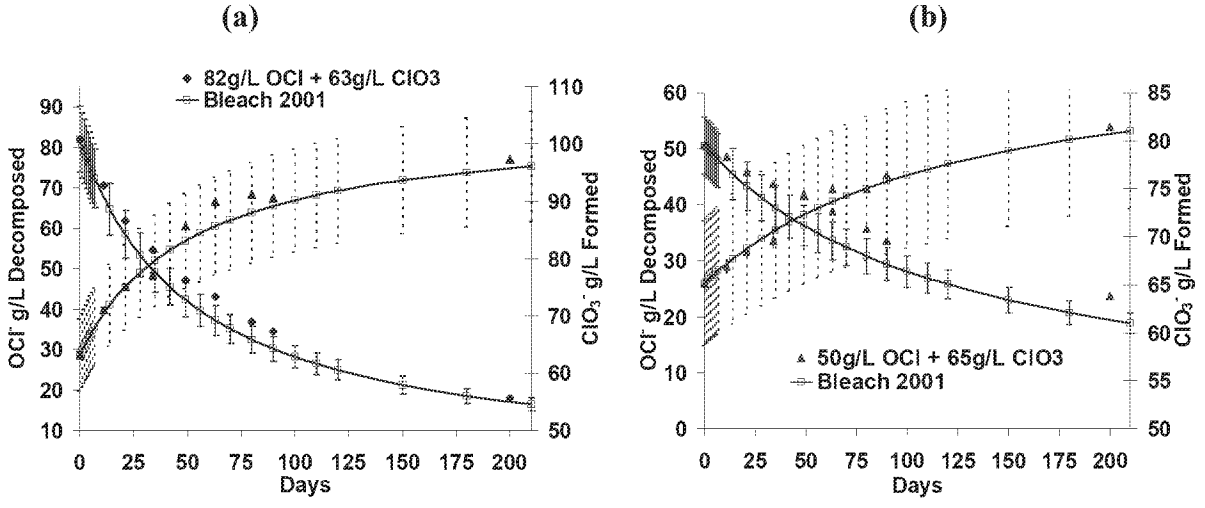

Figure 4.10 Overlaid plot of hypochlorite decomposition and chlorate formation at 30 °C (a) initial concentration of OCl^- = 82g/L (b) Initial concentration of OCl^- = 50g/L

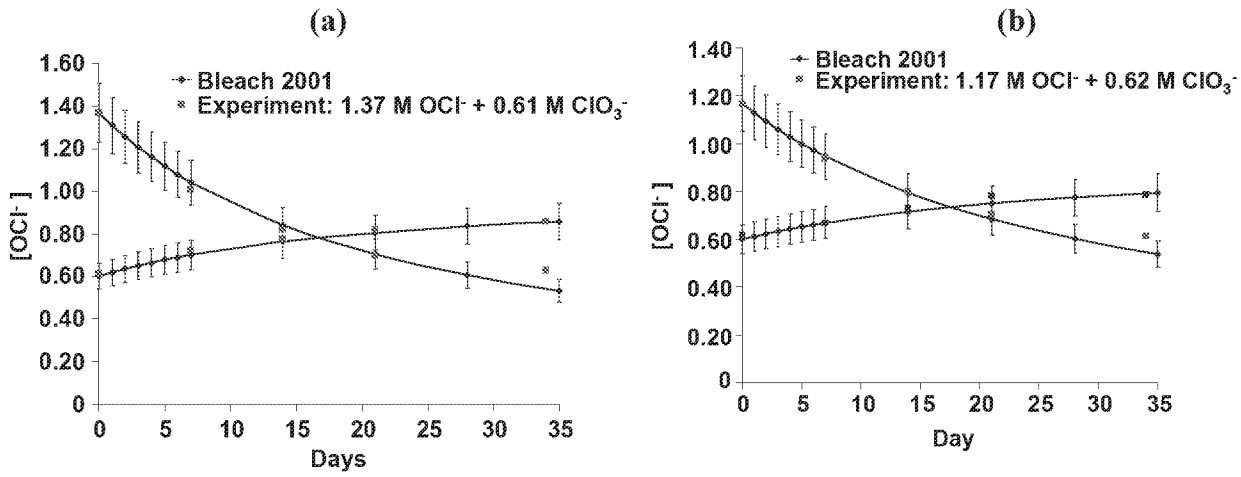

Figure 4.11 Overlaid plot of hypochlorite decomposition and chlorate formation at 40 °C (a) initial concentration of OCl^- = 1.37M (b) Initial concentration of OCl^- = 1.17M

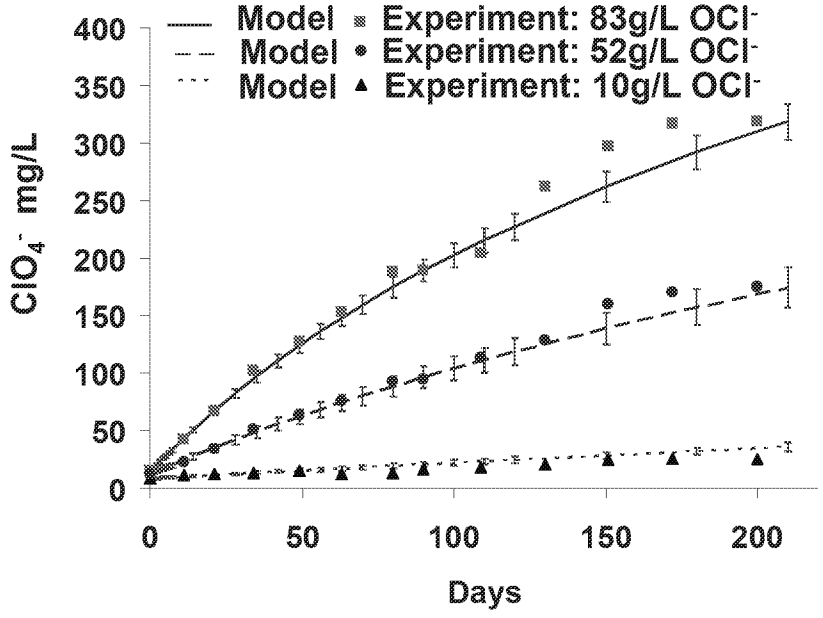

Figure 4.12 Overlaid plot of perchlorate formation experiment vs. predicted at 30 °C

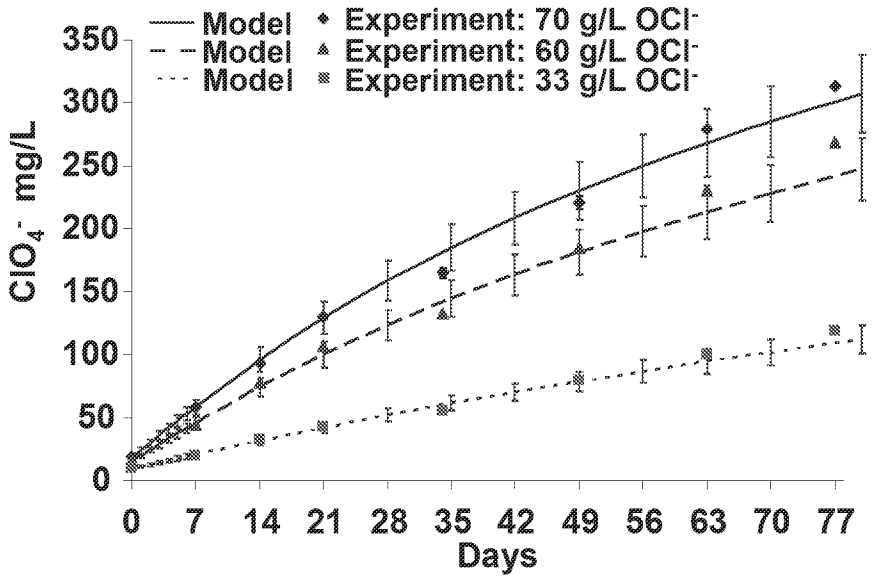

Figure 4.13 Overlaid plot of perchlorate formation experiment vs. predicted at 40 °C

The data shown in Figures 4.12 and 4.13 indicate agreement of 10% or better between observed perchlorate concentration and measured perchlorate concentration in most cases over the entire period of the holding studies. The agreement between experimentally and predicted perchlorate concentrations supports the conclusion that the formation of perchlorate is a second order reaction (first order in hypochlorite and chlorate) that is highly dependent upon ionic strength and temperature. Furthermore, the detailed chemical rate law provided the basis for the "Predictive Model" which not only provides initial rate constants but can also be used in conjunction with *Bleach 2001* to accurately predict perchlorate concentrations as a function of time.

IMPLICATIONS

While the detailed chemical rate law is the key to understanding how factors impact the formation of perchlorate in hypochlorite solutions and can be used to predict perchlorate concentration over time, the primary goal of the "Predictive Model" is really to provide a quantitative platform from which to develop strategies that can be used to minimize perchlorate formation in hypochlorite solutions. As such, a series of hypothetical bulk hypochlorite solutions (starting concentration of 2 M OCl^- or approximately 13% FAC[1]) were used to examine how factors such as dilution and temperature might impact the amount of perchlorate formed in solution over time. Thus, Tables 4.6 – 4.8 were constructed as an aid to understand how the rate of perchlorate formation changes as a function of hypochlorite concentration, temperature, and ionic strength.

The calculations shown in Table 4.6 indicate that dilution by half causes a reduction in rate by a factor of approximately seven and dilution by 10-fold causes reduction in rate of perchlorate formation by a factor of 270. Cooling the hypochlorite solutions also provides

[1] As a point of reference for discussion, a bulk hypochlorite solution of 13% FAC typically equates to approximately 2 M OCl^-, or 103 g/L OCl^-, or 149 g/L NaOCl, or 13.6% NaOCl (depending on the specific gravity).

significant reduction in the rate of perchlorate formation: Cooling by just 5 °C provides approximately a 2-fold reduction in the rate of perchlorate formation, as can be seen in Table 4.7. Preserving hypochlorite from decomposition is also achieved by dilution and cooling. Thus, strategies preserving hypochlorite from decomposition, such as dilution and reduction in temperature, are also the most effective for mitigation of perchlorate formation. Table 4.8 provides a quantitative analysis of how a combined strategy of dilution and temperature reduction can slow the rate of perchlorate formation across a range of scenarios. For example, a dilution of 1:2 and a reduction of storage temperature by 10 °C can provide a 27-fold reduction in the rate of perchlorate formation. A dilution of 1:4 with the same temperature reduction would result in 140 times slower perchlorate formation. Thus, while temperature is important in reducing perchlorate formation, it requires much more cooling to achieve the same effect as simple 1:2 or 1:4 dilutions.

Table 4.6
Predicted rate constants and Rates of perchlorate formation at variable ionic strength and temperature using the "Predictive Model"

T (°C)	[OCl-] (M)	[ClO3-] (M)	I (M)	pH	*Bleach 2001* OCl^- $t_{1/2}$, (days)	k_{calc}, (M^{-1} d^{-1})	Calculated Rate = $[ClO_4^-]/dt$, (M/d)	*Days to reach 10uM ClO_4^-
10	2.00	0.050	6.00	12.0	1319	1.02E-06	1.02E-07	98
10	1.00	0.025	3.00	12.0	5310	5.93E-07	1.48E-08	680
10	0.20	0.005	0.60	12.0	46471	3.84E-07	3.84E-10	26000
15	2.00	0.050	6.00	12.0	610	2.19E-06	2.19E-07	46
15	1.00	0.025	3.00	12.0	2457	1.27E-06	3.18E-08	320
15	0.20	0.005	0.60	12.0	21499	8.22E-07	8.22E-10	12000
20	2.00	0.050	6.00	12.0	290	4.57E-06	4.57E-07	22
20	1.00	0.025	3.00	12.0	1167	2.65E-06	6.63E-08	150
20	0.20	0.005	0.60	12.0	10209	1.72E-06	1.72E-09	5900
25	2.00	0.050	6.00	12.0	141	9.32E-06	9.32E-07	11
25	1.00	0.025	3.00	12.0	577	5.41E-06	1.35E-07	74
25	0.20	0.005	0.60	12.0	4968	3.50E-06	3.50E-09	2900
30	2.00	0.050	6.00	12.0	70	1.86E-05	1.86E-06	5.4
30	1.00	0.025	3.00	12.0	283	1.08E-05	2.69E-07	37
30	0.20	0.005	0.60	12.0	2475	6.96E-06	6.96E-09	1400
35	2.00	0.050	6.00	12.0	36	3.61E-05	3.61E-06	2.8
35	1.00	0.025	3.00	12.0	144	2.10E-05	5.24E-07	19
35	0.20	0.005	0.60	12.0	1261	1.36E-05	1.36E-08	740

*All predictions based on starting perchlorate concentration of 1 µM; Note that the model has not been validated with experimental evidence below 30 °C, thus values in this table should be used only as an indication of trends.

Table 4.7
Summarized effects of dilution and temperature on decomposition of hypochlorite and Rate of formation of perchlorate

Dilution:	$-d[OCl^-]/dt$ (%)	x slower	$d[ClO_4^-]/dt$ (%)	x slower
1:1	100.0	1	100.0	1
1:2	24.8	4.0	14.5	7
1:10	2.8	35.2	0.4	266

Temperature:	$-d[OCl^-]/dt$ (%)	x slower	$d[ClO_4^-]/dt$ (%)	x slower
35 °C	100	1	100	1
30	51	2.0	51	1.9
25	25	3.9	26	3.9
20	12	8.1	13	7.9
15	5.9	17	6.1	17
10	2.7	37	2.8	35

Table 4.8
Detailed table of dilution and temperature effects on the relative Rate of perchlorate formation (assumes starting temperature is 35 °C at ΔT = 0)

Dilution Factor:	1	1:2	1:4	1:6	1:10
Ionic Strength:	6.00	3	1.5	1	0.6
$[ClO_3^-]$ (M):	0.05	0.025	0.013	0.008	0.005
[OCl-] (M):	2.03	1.013	0.506	0.338	0.203
% FAC:	**13.05**	**6.53**	**3.26**	**2.18**	**1.31**
ΔT °C	**Reduction (X-Fold) in Rate of Perchlorate Formation**				
0	1.0	6.9	36	89	270
-1	1.1	7.9	41	100	300
-2	1.3	9.0	47	120	350
-3	1.5	10	54	130	400
-4	1.7	12	62	150	450
-5	1.9	13	71	170	520
-6	2.2	15	81	200	590
-7	2.6	18	93	230	680
-8	2.9	20	110	260	780
-9	3.4	23	120	300	900
-10	3.9	27	140	350	1000
-11	4.5	31	160	400	1200
-12	5.1	35	190	460	1400
-13	5.9	41	210	530	1600
-14	6.8	47	250	610	1800
-15	7.9	54	290	700	2100
-16	9.1	63	330	810	2400
-17	11	73	380	940	2800
-18	12	84	440	1100	3300
-19	14	98	510	1300	3800
-20	17	110	600	1500	4400

SUMMARY OF INSTRUCTIONS FOR USER APPLICATION OF THE "PREDICTIVE MODEL"

While the creation of a graphical user interface-based computer program for implementation of the predictive model was outside of the scope of this study, there are a few simple steps that can be taken to use the model directly. This section of the Report is designed to provide a simplified step-by-step set of instructions for application of the model. In order to use the predictive model, a copy of the *Bleach 2001* software is required. Such software is available from the Water Research Foundation. Additionally, this discussion assumes that the user will have a basic knowledge and understanding of how to use a spreadsheet software package such as Microsoft Excel and how best to organize data within that program. The steps to use the model are outlined below:

1. The user must know the following information about the hypochlorite solution under consideration:
    a. The initial/starting concentration (in mol/liter) of hypochlorite ion, chlorate ion, and perchlorate ion.
    b. If the concentration of perchlorate is unknown, assume "zero" for simplicity. This will lead to an underestimation of the actual perchlorate concentration but will still be useful for determining impacts of dilution and temperature variation.
    c. Ionic strength (in mol/liter). This should be measured using a conductivity probe and converted to ionic strength using Equation 2.12.
    d. The temperature at which the solution will be stored (in Kelvin).
    e. The pH of the hypochlorite solution.

2. Using *Bleach 2001* input the values for temperature, pH, hypochlorite ion concentration, and chlorate ion concentration. Allow *Bleach 2001* to calculate all other parameters. *Bleach 2001* will return a list of hypochlorite ion and chlorate ion concentrations for a specified number of days. These data should be placed into a separate spreadsheet program such as Microsoft Excel. Using a spreadsheet software package will facilitate copying formulas between worksheet cells, making the calculations simpler to repeat under varying conditions.

3. Use Equation 4.14 to calculate the rate constant (k_{calc}) for the ionic strength and storage temperature of the hypochlorite solution in question. The term "R" is the ideal gas law constant which is 8.314 J/K·mol. The term "I" is the measured ionic strength of the hypochlorite solution (mol/L). The term "T" is temperature in Kelvin (K = °C + 273). The units of the calculated rate constant (k_{calc}) will be in L/mol/second. Note that Equation 4.14 actually return the $\log(k_{calc})$, thus the user must convert to k_{calc}.

4. Convert k_{calc} into a "per day" unit: multiply k_{calc} (L/mol/sec) by a factor of 86,400 (60 seconds × 60 minutes × 24 hours) to convert to k_{calc} (L/mol/day).

5. Next, the predicted rate of perchlorate formation needs to be calculated for every incremental (per day) change in hypochlorite and chlorate ion concentration as predicted from *Bleach 2001*. Therefore, using a spreadsheet software package, Equation 4.15, and the hypochlorite and chlorate ion concentration at each increment of days (e.g., days 1, 2, 3, 5, 10, 25, 50, 100, 200), plug in the value for k_{calc}, $[OCl^-]$, and $[ClO_3^-]$ to predict the rate of perchlorate formation. The units of the rate prediction will be in mol/L/day and represents the change in perchlorate concentration per unit time.

6. Finally, the rate of perchlorate formation needs to be converted to a concentration value. This involves several steps:
    a. Input the initial (measured) concentration of perchlorate ion at day "zero" into a spreadsheet cell associated with time = zero days. If the initial concentration of perchlorate ion is unknown, use zero mol/L.
    b. For each calculated rate, multiply the rate by the number of days and add that to the predicted concentration. For example, to predict the change in perchlorate ion concentration from Day 0 to Day 1, the predicted perchlorate ion concentration at Day 1 = $Rate_{(at\ Day\ 1)} \times 1\ Day + [ClO_4^-]_{(at\ Day\ 0)}$.
    c. For a longer time increment (such as Day 10 to Day 25), simply adjust the number of days: the predicted perchlorate ion concentration at Day 25 = $Rate_{(at\ Day\ 10)} \times 15\ Days + [ClO_4^-]_{(at\ Day\ 10)}$.
    d. Continue step-wise until the perchlorate ion concentration has been calculated to the desired number of days.
    e. To convert from mol/L to µg/L, multiply the molarity of perchlorate by 99.5 g/mol $\times 10^6$ µg/g

SUMMARY

Variation in ionic strength proved to be a significant factor impacting the rate of perchlorate formation. Establishing a relationship between the rate constant based on first order of the reaction in both hypochlorite and chlorate (second order overall) combined with ionic strength at different temperatures allowed predictions of rate constant to be made using the detailed chemical rate law described by Equation 4.14. The predicted values of the rate constant agree reasonably with the experimental values, with percent error of 2.1% for 30 °C, 17.7% for 40 °C and 6.75 for 50 °C. Thus investigation of higher order reaction pathway was not applicable. This "Predictive Model" was used to predict rate constants for hypochlorite solutions varying by ionic strengths, temperatures, and concentration of hypochlorite. The predicted rate constants were used to predict initial rates of perchlorate formation, and thus the effects of dilution, temperature reduction were evaluated and strategies to mitigate perchlorate formation proposed.

REFERENCES

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CHAPTER 5
MONITORING OF PERHLCORATE AND OTHER CONTAMINANTS IN HYPOCHLORITE SOLUTIONS

APPROACH

Given that sodium hypochlorite solutions contain contaminants such as chlorite, chlorate, perchlorate, and bromate, this portion of the study was designed (1) to examine the differences in contaminant concentration and formation between sources of hypochlorite solutions and (2) to examine the impact of those solutions on finished and distribution system water quality. Eight utilities were asked to provide samples of hypochlorite solutions (if available), to provide raw water, finished water, and distribution system samples, and to provide qualitative information regarding sources of hypochlorite, storage conditions, etc. In cases where distribution system samples were unavailable, simulated distribution system (SDS) studies were performed. Additionally, samples of brine and hypochlorite solutions from 12 on-site generator (OSG) systems made by three different manufacturers were also provided. Duplicate samples were provided from each site/source, one quenched with malonic acid at the utility upon collection, one unquenched but cooled to 4 °C. All of the hypochlorite solutions, brine, and water samples were analyzed for perchlorate, chlorate, hypochlorite, bromate, and dissolved transition metals (Co(II), Cu(II), Fe(III), Ni(II), and Mn(II)). Hypochlorite solution samples were also aged at 50 °C to measure the rate of hypochlorite decomposition and contaminant formation during a 30-day incubation study.

The quantitative data obtained from the analysis of the fresh and aged hypochlorite solution samples was used to assess potential impacts on finished water and to validate the "Predictive Model" developed from the detailed chemical rate law and described in Chapter 4. First, the maximum use level (MUL) approach described by NSF (NSF/ANSI 2005) was used to predict potential impacts on finished water quality. Next, the *Bleach 2001* program (Adam, Gordon, and Pierce 2001) was used to compare measured hypochlorite decomposition and chlorate formation during the incubation study with the predicted decomposition and formation by *Bleach 2001*. By comparing actual and predicted values, some insight into other possible factors (e.g., metal ions) that may have been impacting decomposition was possible. Finally, the predicted daily concentration of hypochlorite and chlorate from *Bleach 2001* was combined with the "Predictive Model" developed in Chapter 4 of this report to predict perchlorate concentration on a daily basis. Comparing the "Predictive Model" perchlorate concentration with the measured concentration of perchlorate in the aged hypochlorite samples provided additional validation of its applicability to bulk hypochlorite solutions other than those used for development of the detailed chemical rate law.

DESCRIPTION OF UTILITIES AND OSG SYSTEMS

As part of this research study, eight utilities agreed to participate by sending hypochlorite and water samples from the treatment process. Of those utilities, 5 used bulk hypochlorite, 2 used OSG hypochlorite, and 1 used chlorine gas. The participating utilities represented six states and two countries: AZ, CA, FL, GA, NV, OH, and Japan. One participating utility (Utility 8) was a wastewater treatment plant that uses bulk hypochlorite for disinfection of water for non-

potable reuse. Utility 8 represents the only wastewater plant incorporated into the study and was chosen as a "challenge" water to determine whether the more complex matrix could impact perchlorate formation in a simulated distribution system study (SDS). The Japanese site (Utility 3) was sampled during the method development stage of the project but was not re-sampled due to recent data regarding perchlorate in Japan (Asami, Kosaka, and Kunikane 2007; Kosaka 2007; Asami, Kosaka, and Kunikane 2009). The relevant utility descriptions are summarized in Table 5.1.

In addition to the utilities that participated in this study, two large suppliers of OSG systems agreed to supply hypochlorite solutions from ten additional OSG locations and/or systems, providing a total of 12 OSG hypochlorite samples including the two from the participating utilities. A description of the OSG systems is provided in Table 5.2. OSG 9 and 10 are cross-referenced with those in Table 5.1. All OSGs tested used an electrolytic conversion of a brine solution to hypochlorite.

Table 5.1
Information on utilities sampled, age of hypochlorite, and water source

Utility	Hypo source	Sampling date	Hypochlorite age	Water source*
Utility 1-A	Bulk	1/21/2009	60% 90 day-old, 40% 7 day-old	SW
Utility 1-B, OSG 9	OSG 9	1/21/2009	2 days since production	SW
Utility 2	Bulk	1/26/2009	34 days	SW
Utility 3	Bulk	Not Sampled	Not Sampled	Japan, SW
Utility 4	Cl_2 Gas	1/20/2009	N/A	GW, Riverbank Filtration
Utility 5	Bulk	1/26/2009	≥ 5 days	GW
Utility 6, OSG 10	OSG 10	1/29/2009	< 1 day	SW
Utility 7	Bulk	2/7/2009	≥ 12 days	OD, SW, GW
Utility 8	Bulk	1/27/2009	1 to 8 days	WW

*Water sources: SW = Surface Water, GW = Groundwater, OD = Ocean Desalination, WW = Tertiary treated wastewater for non-potable reuse

Table 5.2
Description of on-site generators (OSG), identification numbers, and salt source

OSG Model	Anode Material*	OSG Capacity (PPD)	OSG Energy (kWh/lb FAC)	Years of Service	Salt Source
1a	DSA	24	2.0	4	Unknown
1b	DSA	2,000	2.0	10	Unknown
2a	DSA	75	2.0	4	Unknown
2b	DSA	450	2.0	3	Unknown
3	DSA	750	2.0	1	Unknown
4	DSA	300	2.0	2	Unknown
5	DSA	400	2.0	**	>99.7% as NaCl
6	DSA	180	3.5	**	>99.7% as NaCl
7	DSA	20	3.3	**	>99.5% as NaCl
8	DSA	10	5.2	**	>99.5% as NaCl
9	DSA	1200	Unknown	3	>96% as NaCl
10	DSA	2,000	1.6 to 2.0	2.5, 6.5	>99.7% as NaCl

*Dimensionally Stabilized Anode (DSA), likely titanium; **OSG units only used at factory for testing, thus had << 1 year service time; *** No other information provided

Finally, one supplier of calcium hypochlorite agreed to provide freshly manufactured calcium hypochlorite in solid form. Little is known about the formation of perchlorate in solid hypochlorite, but the Project Team wanted to determine if there was perchlorate present from the manufacturing process and whether dissolved calcium hypochlorite would age any differently than sodium hypochlorite. While it is understood that calcium hypochlorite is not commonly stored in dissolved form and is typically used immediately upon dissolution, it was decided that dissolved calcium hypochlorite would be aged as a comparison to determine whether there was some other contaminant (e.g., chloride) that could potentially impact perchlorate formation. Thus, with the utility hypochlorite solutions and OSG samples, calcium hypochlorite was also aged at 50 °C for a period of 30 days using nominal concentrations of 3% and 6% FAC.

RESULTS

Contaminants in Bulk, OSG, and Calcium Hypochlorite Solutions

The concentration of hypochlorite, perchlorate, chlorate, and bromate in the bulk samples for each of the 8 utilities is shown in Table 5.3.

- Only Utility 1-A appeared to have significant impacts on finished water concentration from the perchlorate levels in the bulk hypochlorite. The low FAC concentration at Utility 1-A (compared with other bulk hypochlorite solutions tested) and the high levels of perchlorate and chlorate could be explained by the age of the hypochlorite solution which was a mixture of 90-day old (60%) and 7-day old (40%) bulk hypochlorite.

- None of the utilities were above California's 6 µg/L MCL for perchlorate and only two were above Massachusetts's 2 µg/L MCL.

- Chlorate contamination from the hypochlorite solutions appeared to impact all of the utilities tested. Of those utilities, three had concentrations of chlorate in the finished drinking water above the 800 µg/L notification level in California and an additional utility was at the proposed 200 µg/L action level recommended in CA (Howd 2002).

- Bromate was observed at mg/L levels in all bulk hypochlorite solutions, though none of the utilities tested had finished water concentrations over the 10 µg/L bromate MCL mandated by the US EPA.

Table 5.3
Summary of perchlorate, chlorate, and bromate concentrations in raw water, finished water, and hypochlorite used at participating utility locations

			ClO_4^-			ClO_3^-			BrO_3^-		
Utility	Source	FAC (g/L)	Hypo (µg/L)	Raw (µg/L)	Fin. (µg/L)	Hypo (mg/L)	Raw (mg/L)	Fin. (mg/L)	Hypo (µg/L)	Raw (µg/L)	Fin. (µg/L)
1-A	Bulk	87	14,000	<0.5	3.6	19,000	0.014	0.58	24,000	<0.5	0.5
1-B	OSG 9	6.8	3,500	<0.5	<0.5	480	0.026	1.5	2,700	<0.5	3.6
2	Bulk	150	670	<0.5	<0.5	5,900	0.005	0.019	30,000	<0.5	<0.5
4	Cl_2 Gas	n/a	n/a	<0.5	<0.5	n/a	<0.003	<0.003	n/a	<0.5	<0.5
5	Bulk	120	220	<0.5	<0.5	1,800	0.13	0.20	9,000	1.3	1.4
6	OSG 10	8.7	19	2.0	2.1	380	0.008	0.16	<100	<0.5	1.3
7	Bulk	120	230	<0.5	<0.5	2,400	<0.003	0.13	9,900	<0.5	0.92
8	Bulk	130	2,000	1.6	1.2	8,000	<0.003	0.79	7,700	<0.5	2.6

Hypo = Hypochlorite solution; Raw = Raw water entering the treatment plant; Fin = Finished water leaving treatment plant; Samples analyzed in duplicate measurements, with average % difference for: ClO_4^- 2.0%, BrO_3^- 4.2%, and ClO_3^- 2.5%.

The OSG samples also had high variations in FAC, chlorate, and perchlorate concentrations as shown in Table 5.4. All samples labeled "quenched hypochlorite" were collected at the utility in bottles pre-dosed with malonic acid. Non-quenched samples were cooled to 4 °C and shipped with the quenched samples to the laboratory at SNWA via overnight delivery. Samples were collected directly from the OSG when possible; otherwise they were collected from dosing tanks/day tanks. The solution for OSG 9 was at least 48 hours old when collected and may have been stored at temperatures up to 42 °C. The brine solution and feed water for OSG 9 were at 40 to 42 °C prior to electrolytic conversion.

- Most OSGs had less than 700 µg/L chlorate present in the finished product.

- Bromate concentration ranged from 0.2 mg/L to 6 mg/L. Bromate concentrations are limited by the amount of bromide (which is rapidly converted to bromate in

hypochlorite solutions) and is likely related to the amount of bromide present in the salt and/or feed water used for hypochlorite generation.

- There were no discernable trends in the amount of perchlorate or chlorate formed by any given OSG with respect to energy consumption, OSG production capacity (pounds per day), or actual FAC concentrations.

Table 5.4
Chlorate, bromate, and perchlorate data for quenched and non-quenched samples and the feed brine to the OSG

	Quenched hypochlorite				Non-quenched hypochlorite				Brine		
OSG Model	ClO_3^- (mg/L)	BrO_3^- (mg/L)	ClO_4^- (µg/L)	FAC, (g/L)	ClO_3^- (mg/L)	BrO_3^- (mg/L)	ClO_4^- (µg/L)	FAC, (g/L)	ClO_3^- (mg/L)	BrO_3^- (mg/L)	ClO_4^- (µg/L)
1a	89	0.15	*	<0.1	140	4.1	5.4	9.7	<0.5	<0.1	<2.5
1b	320	3.0	15	2.9**	240	3.8	16	8.0	<0.5	<0.1	<2.5
2a	57	0.47	8.2	<0.1	97	5.3	8.6	6.8	<0.5	<0.1	<2.5
2b	450	2.7	380	2.6**	360	3.3	410	6.9	<0.5	<0.1	<2.5
3	240	1.7	6.6	<0.1	270	4.4	7.3	10	<0.5	<0.1	<2.5
4	1000	2.1	39	<0.1	1200	2.6	40	4.5	<0.5	<0.1	<2.5
5	220	1.1	31	<0.1	260	2.6	31	8.0	<0.5	<0.1	<2.5
6	180	0.54	21	<0.1	180	1.4	22	5.2	<0.5	<0.1	<2.5
7	610	0.32	79	<0.1	750	2.0	83	7.2	2.0	<0.1	<2.5
8	180	0.10	660	<0.1	240	0.71	740	3.6	2.1	<0.1	<2.5
9	510	5.3	3100	<0.1	760	5.7	3500	6.8	7.2	<0.1	65
10	450	0.13	19	<0.1	780	0.15	19	8.7	<0.5	<0.1	<2.5

*Sample contaminated, no perchlorate data available for unquenched hypochlorite; **Too much sample was added to the bottle provided with pre-dosed quenching agent, thus quenching was not complete

Transition metal ion concentrations measured for this study were low in most of the bulk hypochlorite (Table 5.5), OSG (Table 5.6), and brine samples (Table 5.7), though Utility 1-A had nickel present at 0.2 mg/L, copper at 0.1 mg/L and iron concentrations approaching 10 mg/L in the hypochlorite solution itself. As metals have been shown in earlier chapters and elsewhere to have a catalytic effect on the decomposition of hypochlorite, the presence of iron and nickel may have been a factor (in addition to age) in the low FAC concentration at Utility 1-A. Regarding the OSG hypochlorite, most brine samples showed higher levels of metal ion contamination relative to the hypochlorite product from the OSG. This difference is likely due to loss of metals to reduction and/or plating on the anode of the electrolytic cell. Current hypochlorite specifications recommend <0.1 mg/L iron and <0.05 mg/L nickel, copper, and cobalt (Gordon and Bubnis 2000). The bulk hypochlorite sampled from Utilities 1-A, 5, 7, and 8 all contained at least one contaminant above the specified levels.

Table 5.5
Concentrations of transition metals in utility bulk hypochlorite samples

Utility	Mn	Fe	Co	Ni	Cu
			(µg/L)		
1-A	<100	9200	<100	200	110
1-B, OSG 9	<100	<1250	<100	<100	<100
2	<100	<500	<100	<100	<100
3	n/a	n/a	n/a	n/a	n/a
5	<100	1100	<100	<100	<100
6, OSG 10	<100	<250	<100	<100	<100
7	<100	<500	<100	110	<100
8	<100	2300	<100	<100	<100

Table 5.6
Concentrations of transition metals in OSG hypochlorite solutions

OSG	Mn	Fe	Co	Ni	Cu
			(µg/L)		
1a	<25	<125	<25	<25	<25
1b	<25	239	<25	<25	55
2a	<25	172	<25	<25	<25
2b	<25	160	<25	<25	<25
3	<25	120	<25	<25	<25
4	<25	<125	<25	<25	<25
5	<25	<125	<25	<25	<25
6	<25	<125	<25	<25	<25
7	<25	<50	<25	<25	<25
8	<25	<50	<25	<25	<25
9	<100	<125	<100	<100	<100
10	<100	<250	<100	<100	<100

Table 5.7
Concentrations of transition metals in OSG brine solutions

OSG	Mn	Fe	Co	Ni	Cu
			(µg/L)		
1a	45	1293	<25	30	120
1b	33	752	<25	<25	92
2a	50	1100	<25	<25	95
2b	30	630	<25	<25	92
3	29	1200	<25	27	110
4	71	400	<25	29	98
5	<25	160	<25	<25	120
6	<25	<125	<25	<25	83
7	<25	<250	<25	<25	<25
8	<25	<250	<25	<25	<25
9	<25	<125	<25	<25	<25
10	N/A	N/A	N/A	N/A	N/A

Transition metal ions were not measured in the calcium hypochlorite solutions. However, bromate, chlorate, and perchlorate were all measured for the 3% and 6% (as FAC) solutions of calcium hypochlorite immediately after mixing with reagent water. The 3% calcium hypochlorite solution had 390 mg/L chlorate, 27 µg/L perchlorate, and 2.4 mg/L bromate for 32 g/L FAC. The 6% calcium hypochlorite solution had 830 mg/L chlorate, 55 µg/L perchlorate, and 5.3 mg/L bromate for 61 g/L FAC.

Given the data described above, a comparison was made by normalizing all of the contaminant concentrations by the concentration of FAC. Table 5.8 was assembled to show a relative contribution (on a mass of contaminant per mg FAC basis) from each hypochlorite solution. Of the comparisons made within the limited data set collected for this project, the only trend that stands out is that the OSGs consistently contribute more bromate per milligram of FAC than the fresh bulk hypochlorite solutions or the two calcium hypochlorite solutions tested. The higher levels of bromate in the OSG solutions are likely a result of bromide in the feed water and/or salt used to make the brine solutions for electrolysis. Current NSF/ANSI 60 standards recommend no more than 0.5 µg BrO_3^- per mg FAC (NSF/ANSI 2005) in hypochlorite solutions. Based on this limit, three OSG solutions exceed the recommendation and an additional two OSGs approached the limit (0.48 µg BrO_3^- per mg FAC). Neither the calcium hypochlorite sample nor any of the bulk hypochlorite solutions exceeded the current bromate standard. Furthermore, only OSGs 5-8 and OSG 10 used a salt with greater than 99.5% purity (as NaCl), a fact reflected in the lowest overall bromate concentrations. Thus, these data support the use of high quality, low-bromide salts for hypochlorite generation, though further investigations detailing specific recommendations should be performed.

Other than the bromate observation, there are no consistent trends and contaminant concentrations vary widely within and between brands, hypochlorite sources, and production methods. Thus, from this limited data set collected during this project, there does not appear to be a straightforward way to determine what type of *freshly prepared* hypochlorite solution (OSG, bulk, or calcium) would result in the lowest mass loading of contaminants into the finished drinking water which is consistent with OSG and bulk hypochlorite data reported elsewhere (Asami, Kosaka, and Kunikane 2009).

Table 5.8
Relative contribution of specific contaminants on a per-mass-FAC basis

		Concentration in hypochlorite solutions				Mass of contaminant added per mg FAC		
		ClO_3^- (mg/L)	BrO_3^- (mg/L)	ClO_4^- (µg/L)	FAC (g/L)	ClO_3^- (µg/mg FAC)	BrO_3^- (ng/mg FAC)	ClO_4^- (ng/mg FAC)
Bulk	1-A	19,000	24	14,000	87	220	280	160
	2	5,900	30	670	150	39	200	4.5
	4	n/a	n/a	n/a	n/a	n/a	n/a	n/a
	5	1,800	9	220	120	15	75	1.8
	7	2,400	10	230	120	20	83	1.9
	8	8,000	8	2,000	130	62	59	15
OSG	1a	140	4.1	5.4	9.7	14	420	0.6
	1b	240	3.8	16	8	30	480	2.0
	2a	97	5.3	8.6	6.8	14	780	1.3
	2b	360	3.3	410	6.9	52	480	59
	3	270	4.4	7.3	10	27	440	0.7
	4	1200	2.6	40	4.5	270	580	8.9
	5	260	2.6	31	8	33	330	3.9
	6	180	1.4	22	5.2	35	270	4.2
	7	750	2	83	7.2	100	280	12
	8	240	0.71	740	3.6	67	200	210
	9	760	5.7	3500	6.8	110	840	520
	10	780	0.15	19	8.7	90	17	2.2
Cal Hypo	Cal 1	390.0	2.40	27.0	32	12	75	0.8
	Cal 2	830.0	5.30	55.0	61	14	87	0.9

Contaminant Concentrations in Distribution System and SDS Samples

The concentration of perchlorate, chlorate, and bromate was also measured in the distribution system samples in order to determine whether there was any additional chlorate, perchlorate, or bromate formation. In the case of Utility 2, a SDS study was used instead of collecting actual distribution system samples. Distribution system sampling locations were targeted to give a median residence time and a maximum residence time for each utility. Based on the model developed in Chapter 4 and the considerations of hypochlorite ion concentration, temperature, pH, and ionic strength it was not expected that any appreciable formation of chlorate, perchlorate, or bromate would be observed. The results of the distribution system sampling and SDS studies are shown in Table 5.9.

Table 5.9
Perchlorate, chlorate, and bromate concentrations in finished waters and distribution system samples

Utility	Res. time A (hrs)	Res. time B (hrs)	ClO_4^- Fin. (µg/L)	ClO_4^- Dist. A (µg/L)	ClO_4^- Dist. B (µg/L)	ClO_3^- Fin. (mg/L)	ClO_3^- Dist. A (mg/L)	ClO_3^- Dist. B (mg/L)	BrO_3^- Fin. (µg/L)	BrO_3^- Dist. A (µg/L)	BrO_3^- Dist. B (µg/L)
1-A	36	72	3.6	<0.5	3.1	0.58	0.59	1.2	0.5	0.80	2.9
1-B	36	72	<0.5	3.2	3.1	1.5	1.4	1.3	3.6	3.4	2.8
2	72	216	<0.5	<0.5	<0.5	0.019	0.046	0.045	<0.5	<0.5	<0.5
4	96	168	<0.5	<0.5	<0.5	<0.003	<0.003	<0.003	<0.5	<0.5	<0.5
5	36	72	<0.5	<0.5	<0.5	0.20	<0.003	<0.003	1.4	2.1	2.2
6	6	12	2.1	2.2	2.2	0.16	0.14	0.031	1.3	2.6	2.2
7	12	24	<0.5	<0.5	<0.5	0.13	0.13	0.13	0.92	0.80	0.90
8*	100	150	1.2	1.2	0.90	0.79	1.6	0.82	2.6	5.9	3.2

* SDS conducted on wastewater samples instead of collecting actual distribution system samples—sample A had free chlorine residual with no ammonia while sample B had excess ammonia present and thus free chlorine was converted entirely to chloramines

In all cases except Utility 1-A, the concentration of contaminants did not increase in the distribution system. The difficulty in using grab samples from distribution system is that the hypochlorite solution used to disinfect the water is constantly changing and experiences turnover from new shipments and/or on-site generation. Thus, in order to assess behavior of chlorate, perchlorate, and bromate in distribution systems an in-depth study with more sampling sites (and distribution systems) combined with temporal observations over a period of several months is suggested as a future research direction.

Holding Studies for Bulk, OSG, and Calcium Hypochlorite Solutions

Each of the unquenched OSG solutions collected for this study was held at 50 °C for a period of 30 days while periodic aliquots of the solution were collected for analysis of ionic strength, pH, and concentration of hypochlorite, chlorate, perchlorate, and bromate. Data for the oxyhalides were grouped by manufacturer and graphed against holding time (Figures 5.1, 5.2, and 5.3). As expected, samples with high initial hypochlorite concentrations (e.g., OSG 1a and OSG3, Figure 5.1) also showed higher overall perchlorate formation relative to starting concentration and those with low initial hypochlorite concentration (e.g., OSG 4, Figure 5.1) showed the lowest overall perchlorate formation relative to the starting concentration. Measurements of bromate concentration had a high degree of variability because sample dilutions were made to target chlorate and perchlorate; thus, bromate analysis was not optimized for utility OSG and bulk hypochlorite holding study and the data are not shown. However, bromate concentrations in all OSG and bulk hypochlorite samples did not appear to suggest a trend of increasing or decreasing concentration. Such observation is supported in the bromide/bromate studies discussed in Chapter 3 (most bromate formation is likely to occur during on-site generation or very shortly thereafter).

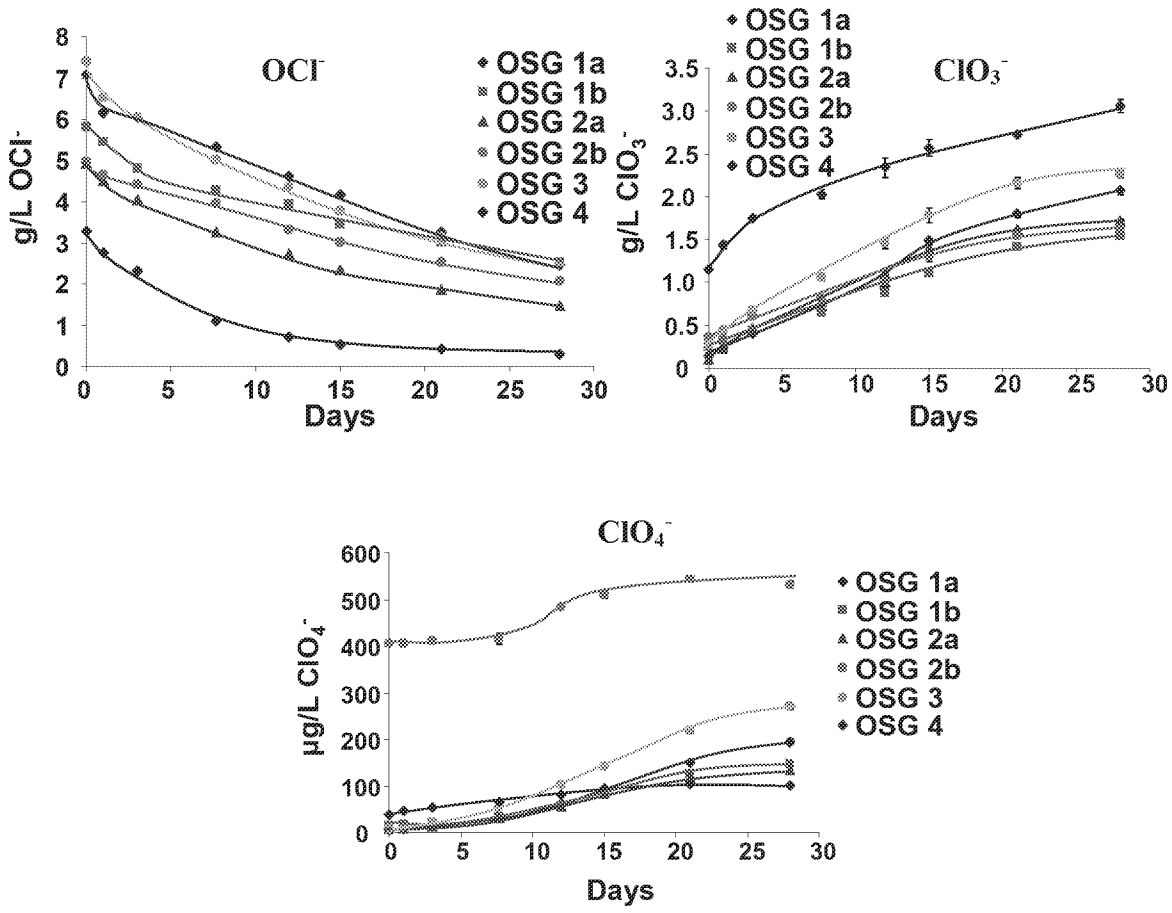

Figure 5.1 Hypochlorite, chlorate, and perchlorate concentrations during 50 °C holding study for six OSG samples from the same OSG manufacturer (different models)

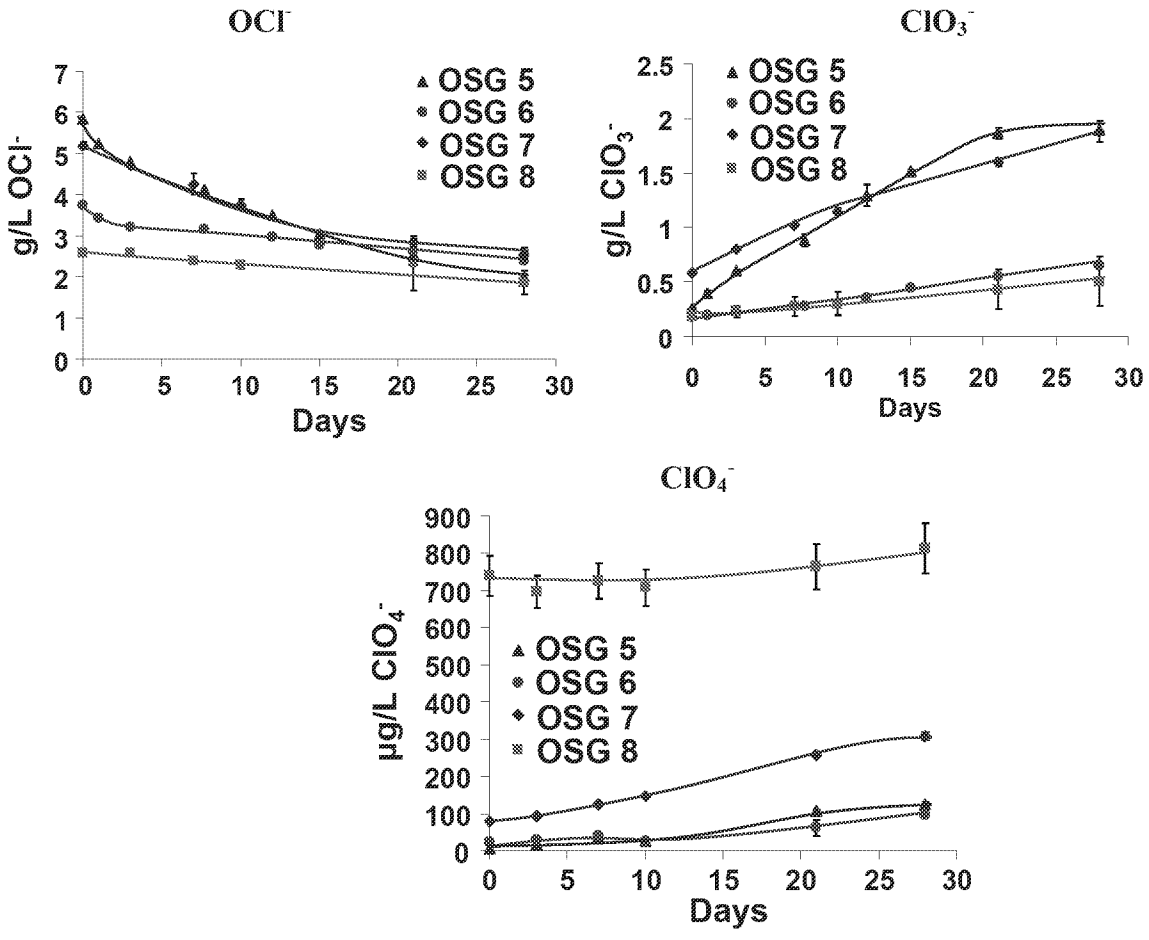

Figure 5.2 Hypochlorite, chlorate, and perchlorate concentrations during 50 °C holding study for 4 OSG samples from the same OSG manufacturer (different models)

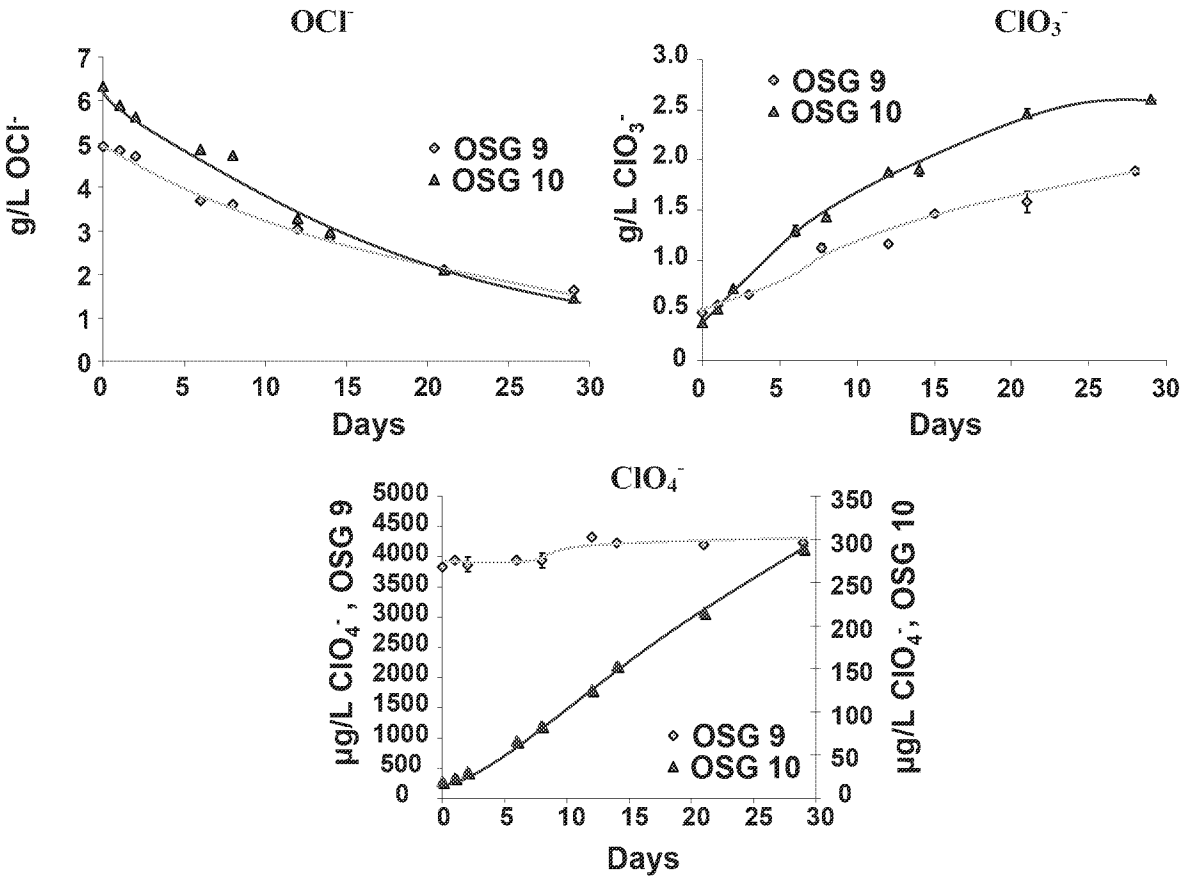

Figure 5.3 Hypochlorite, chlorate, and perchlorate concentrations during 50 °C holding study for the two utility-provided OSG samples

The hypochlorite samples from the utilities were similarly aged at 50 °C and analyzed for changes in hypochlorite, chlorate, perchlorate, and bromate concentrations (Figure 5.4). In all cases a higher initial hypochlorite concentration corresponded to higher rate of chlorate and perchlorate formation. Another interesting observation is the relative magnitude of perchlorate formation in the OSG samples versus the bulk hypochlorite samples. There is significantly less chlorate and perchlorate formation in the aging OSG samples than the aging bulk hypochlorite samples, a fact easily explained by the difference in starting concentration of hypochlorite and predicted by the reaction kinetics.

Similar to the bulk and OSG hypochlorite solutions, the two calcium hypochlorite solutions (3% and 6% FAC) were aged at 50 °C and 60 °C. The data from these two incubation studies are summarized in Figure 5.5. Upon examination of the data there were no major deviations from the trends observed in the bulk and OSG hypochlorite solutions: Increased temperature and increased starting concentration of hypochlorite both increased the rate of chlorate and perchlorate formation.

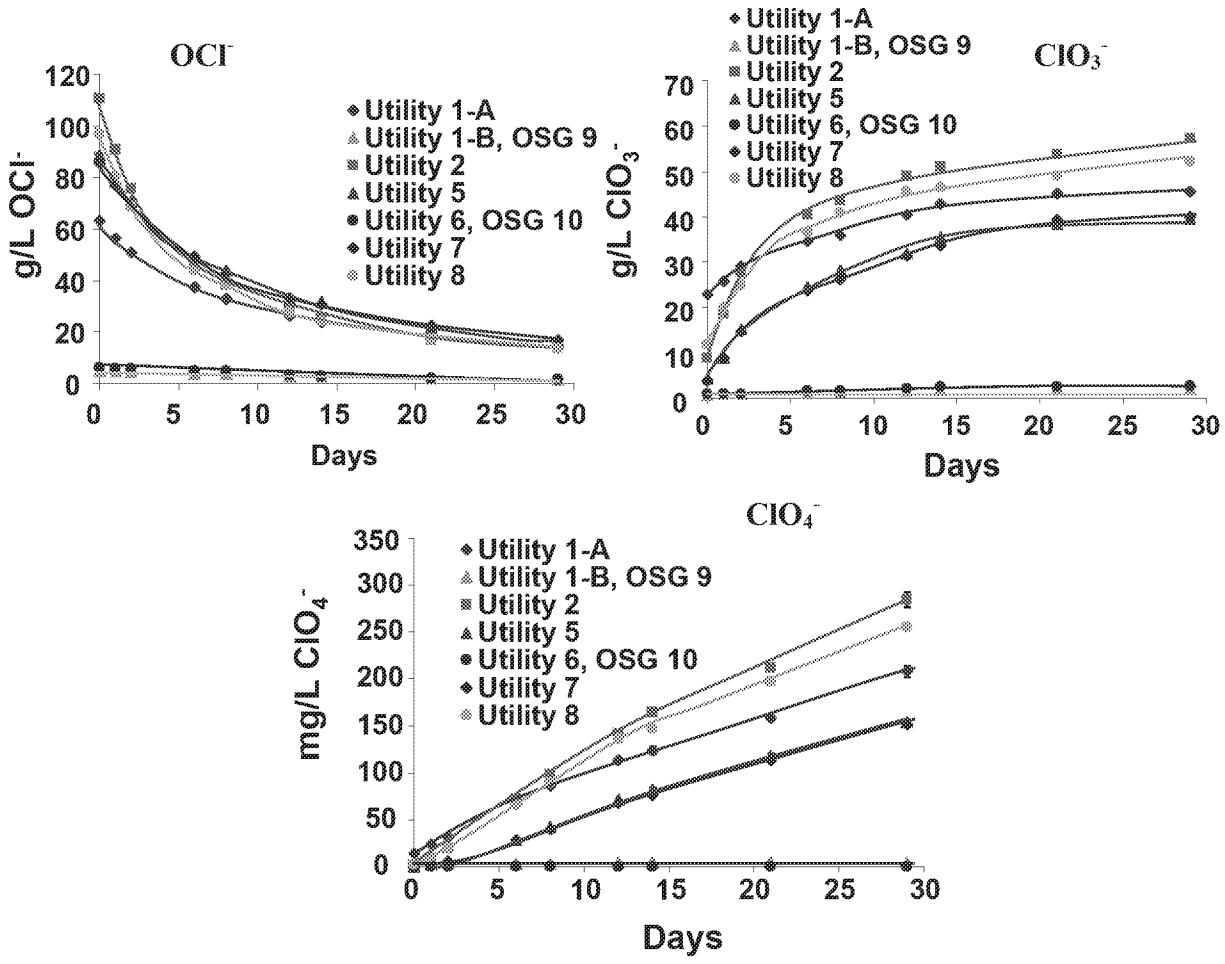

Figure 5.4 Hypochlorite, chlorate, and perchlorate concentrations during 50 °C holding study for all Utility hypochlorite samples

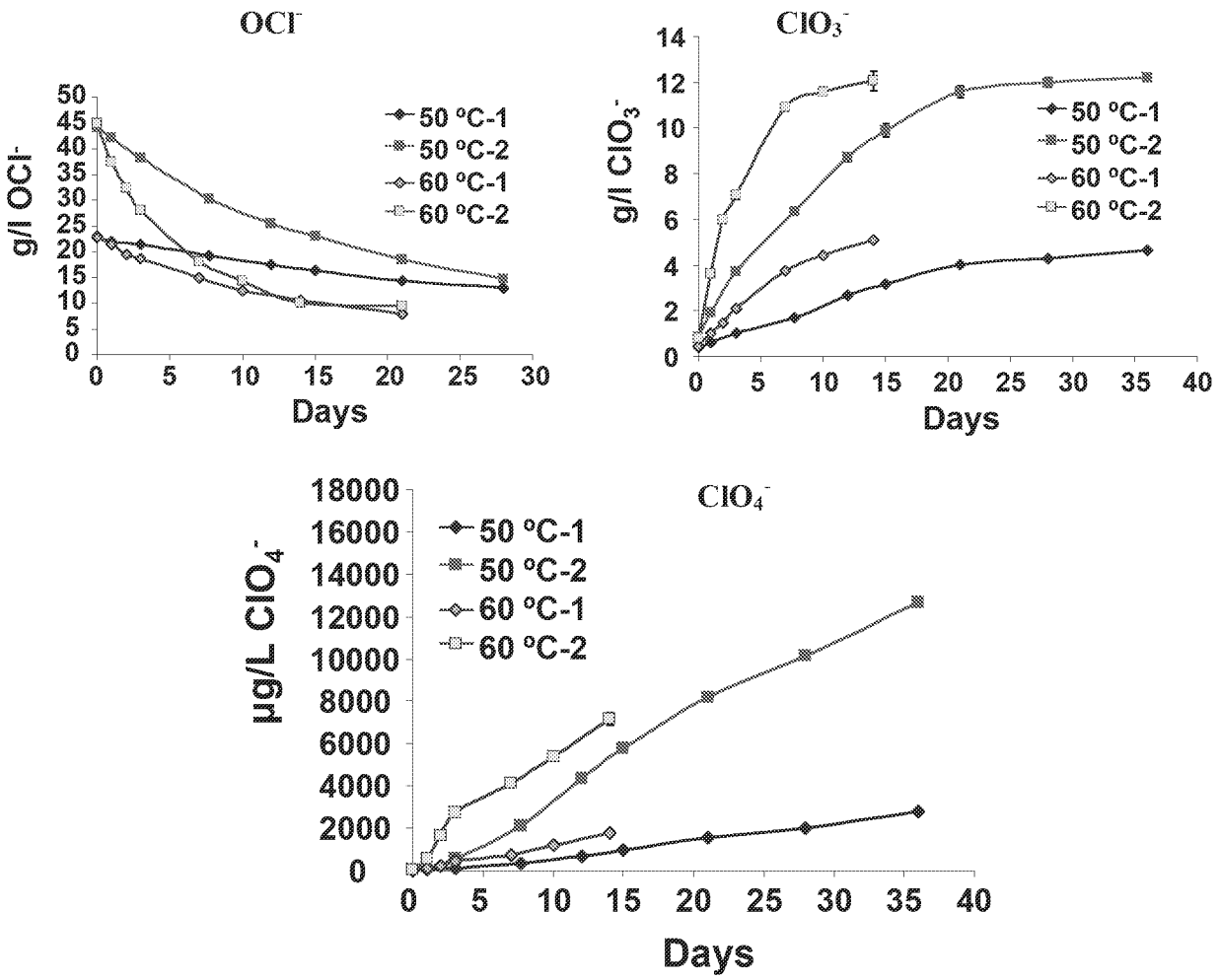

Figure 5.5 Calcium hypochlorite solutions aged at 50 °C and 60 °C with 3% FAC (Cal Hypo 1: 50 °C-1, 60 °C -1) and 6% FAC (Cal Hypo 2: 50 °C-2, 60 °C -2)

Comparison of Measured vs. Predicted Concentration using MUL

The MUL of 10 mg/L was used to estimate the maximum amount of contaminants that could be dosed into the finished water via hypochlorite addition. The calculation of MUL followed the equations listed below and relied upon the measured concentration of specific contaminants (e.g., chlorate, perchlorate, bromate) in the hypochlorite to be dosed into the water plus the concentration of each contaminant in the raw water:

$$\text{Volume}_{\text{hypo dosed}} = \frac{10\,\text{mg/L} \times 1\,\text{L}}{\text{FAC}_{\text{hypo dosed}}\,(\text{mg/L})} \qquad \textbf{(5.1)}$$

$$\text{Max. Conc.}_{\text{MUL,10}} = \frac{\text{Volume}_{\text{hypo dosed}} \times [\text{Contaminant}]_{\text{hypo dosed}}}{1\text{L}} + [\text{Contaminant}]_{\text{raw water}} \qquad \textbf{(5.2)}$$

The maximum expected concentrations of each contaminant based on the MUL approach are listed in Table 5.10. In most cases, the MUL calculated concentrations in the finished water did not match the measured finished water concentrations of chlorate, perchlorate, or bromate though they did provide a conservative estimate. The premise behind the MUL is that it provides for a conservative calculation by *overestimating* the concentration of a contaminant in the finished water by assuming the maximum amount of hypochlorite that would be used at any given facility. While this is a reasonable approach, it is limited in its predictive ability because it does not take into consideration other potential sources of contaminants (e.g., oxidation of bromide to bromate during ozonation) or sinks of contaminants (e.g., ion exchange sites on filter media). Underestimation of contaminant concentrations by >20% occurred 5 times (once for perchlorate, twice for chlorate, twice for bromate). Such observations are consistent with attempts published elsewhere at using injection ratios (similar to MUL but using actual dosing quantities) to predict finished water concentrations of chlorate and perchlorate (Asami, Kosaka, and Kunikane 2007; Asami, Kosaka, and Kunikane 2009). Thus, it is not clear whether using the MUL would be a good tool to predict actual contaminant concentrations in drinking water nor would it be beneficial to use as a "normalization" technique as suggested elsewhere (Greiner, et al. 2008). However, if combined with an understanding of the treatment process at any given facility it may be able to provide a reasonable estimation of maximum expected contaminant concentrations.

Table 5.10
Comparison of measured and calculated concentrations of contaminants in finished water samples from participating utilities

		ClO_4^-			ClO_3^-			BrO_3^-		
Utility	FAC g/L	Hypo (µg/L)	MUL* (µg/L)	Meas.** (µg/L)	Hypo (mg/L)	MUL* (mg/L)	Meas.** (mg/L)	Hypo (µg/L)	MUL* (µg/L)	Meas.** (µg/L)
1-A	87	14000	1.9	3.6	19000	2.2	0.58	24000	3.0	0.5
1-B	6.8	3500	5.4	<0.5	480	0.7	1.5	2700	4.2	3.6
2	150	670	0.3	<0.5	5900	0.4	0.019	30000	2.3	<0.5
4	Cl_2 Gas	n/a	n/a	<0.5	n/a	n/a	<0.003	n/a	n/a	<0.5
5	120	220	0.3	<0.5	1800	0.3	0.20	9000	2.1	1.4
6	8.7	20	2.0	2.1	380	0.4	0.16	50	0.3	1.3
7	120	230	0.3	<0.5	2400	0.2	0.13	9900	1.1	0.92
8	130	2000	1.8	1.2	8000	0.6	0.79	7700	0.8	2.6

*Estimated concentration in finished water based on maximum use level (MUL) of 10 mg/L FAC as Cl_2; **Measured concentration in finished water; Refer to Table 5.3 for raw water concentrations (when raw water concentration was < MRL, a value of ½ the MRL was used in the MUL calculation)

Measured vs. Predicted Concentrations of OCl^- and ClO_3^- in Hypochlorite using *Bleach 2001*

The *Bleach 2001* (Adam, Gordon, and Pierce 2001) model was applied to the aged utility bulk hypochlorite samples for verification that hypochlorite decomposition and chlorate formation was occurring as expected. Four of the five Utility bulk hypochlorite samples were selected for use in this modeling exercise. OSG hypochlorite samples were not used in this exercise as they typically have pH values in the range 9 – 10; the *Bleach 2001* model does not predict below pH 11 because the recommendation for utilities is to store liquid hypochlorite at pH 11 – 13. Thus, running a simulation of OSG hypochlorite decomposition was not applicable. The starting concentration, pH, and holding temperature for the bulk hypochlorite solutions are summarized in Table 5.11. Figure 5.6 shows overlaid plots of hypochlorite decomposition and chlorate formation of measured vs. predicted concentrations for four Utility bulk hypochlorite samples.

Table 5.11
Initial concentrations, pH, and temperature values entered into *Bleach 2001*

Utility	pH	OCl^- (g/L)	ClO_3^- (g/L)	Temperature (°C)
1-A	12.84	63.1	22.8	50
2	13.25	110.7	8.73	50
5	12.90	89.0	4.37	50
8	13.11	96.7	11.6	50

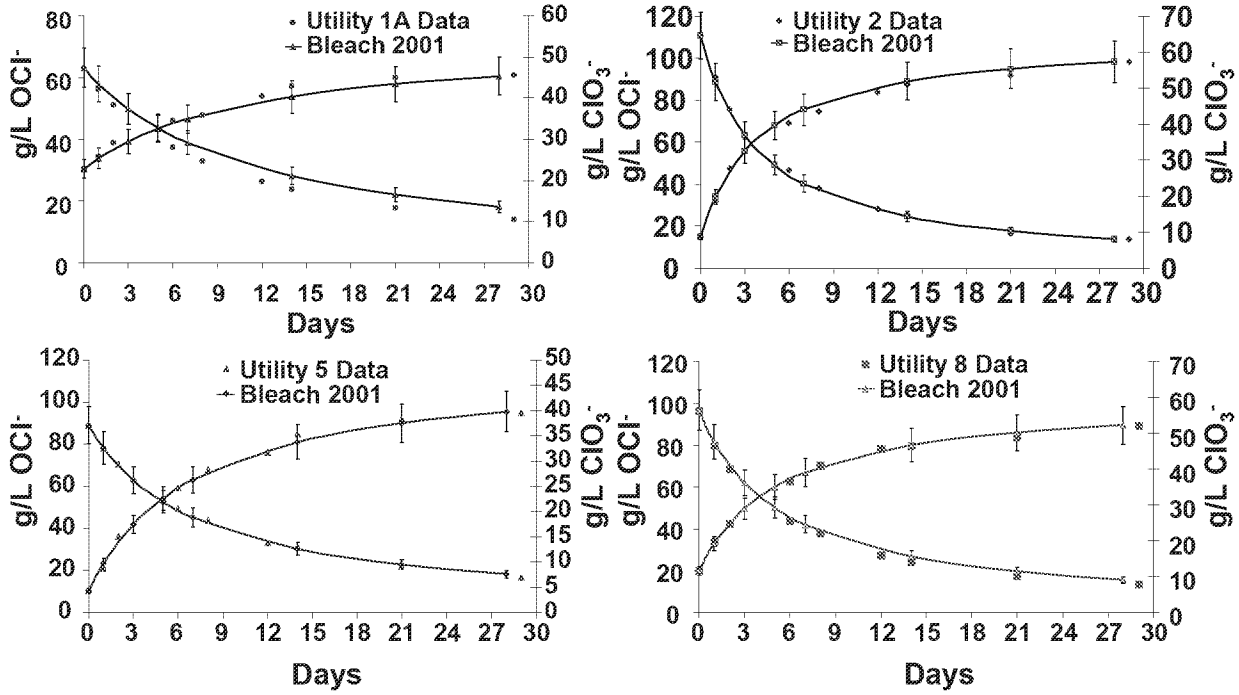

Figure 5.6 Measured vs. predicted concentrations of OCl^- and ClO_3^- in hypochlorite using *Bleach 2001:* Utility 1A, 2, 5, and 8 aged at 50 °C; Error bars are 10% of predicted value

In general, the measured decomposition of sodium hypochlorite samples from the utilities showed excellent agreement (within 5 to 10 %) with the *Bleach 2001* predicted decomposition with the exception of Utility 1-A differing by up to 25%. The plot of the Utility 1-A sample in Figure 5.6 shows that hypochlorite decomposed faster than expected, possibly resulting from the presence of iron at 9.2 mg/L, copper at 0.1 mg/L, and nickel at 0.2 mg/L (Table 5.5) in the hypochlorite solution. Otherwise, the agreement between measured concentrations and predicted concentrations was acceptable. Therefore, considering that the chemical model for predicting perchlorate concentration over time requires an input of predicted hypochlorite and chlorate concentrations, it was determined that *Bleach 2001* could be used to generate those predicted concentrations for use in perchlorate modeling.

Measured vs. Predicted Concentrations of ClO_4^- in Hypochlorite using the "Predictive Model"

The "Predictive Model" from the detailed chemical rate law of perchlorate formation described in Chapter 4 of this report was also applied to the aged bulk hypochlorite samples selected for *Bleach 2001* testing. This application of the "Predictive Model" was used in order to validate its ability to predict perchlorate concentrations in hypochlorite solutions other than those used to develop the model. As an additional exercise, the rate of perchlorate formation and the observed rate constant were calculated for each hypochlorite solution and are summarized in Table 5.12. As seen, the rate of perchlorate formation appears to be impacted by a combination of ionic strength, concentration of hypochlorite, and concentration of chlorate, indicating that each factor is indeed important to include in the "Predictive Model".

Table 5.12
Observed rate and rate constant of perchlorate formation in bulk sodium hypochlorite solutions received from participating utilities

Utility	pH	[OCl-] (mol/L)	[ClO3-] (mol/L)	I (mol/L)	Observed *Rate (x 10^{-6})	**k_{obs} (x 10^{-6})
1-A	12.84	1.226	0.228	5.74	100	363
2	13.25	2.152	0.071	6.47	76	499
5	12.9	1.729	0.022	4.86	19	506
7	13.13	1.661	0.029	4.95	21	427
8	13.11	1.879	0.096	6.26	78	429

*Rate in units of mol ClO_4^- / L / d; **k in units of L / mol ClO_4^- / d
(Utilities 1-B and 6 were OSG samples; Utility 3 was not sampled; Utility 4 used Cl_2 gas)

Comparing the measured concentration of perchlorate over time with the predicted perchlorate concentration provides the best evidence of the validity of the "Predictive Model". Figure 5.7 shows overlaid plots of average measured concentration of perchlorate over time vs. predicted concentration in bulk hypochlorite samples. The error bars in Figure 5.7 have been arbitrarily set at ± 10%. The formation of perchlorate in most samples was predicted to within ± 10% of the actual values. This demonstrates that the "Predictive Model" is a useful way to approximate the formation of perchlorate in bulk hypochlorite solutions. Moreover, this exercise demonstrates that the "Predictive Model" can be used to make specific recommendations to

utilities based on predicted behavior that will assist in minimizing perchlorate formation during storage.

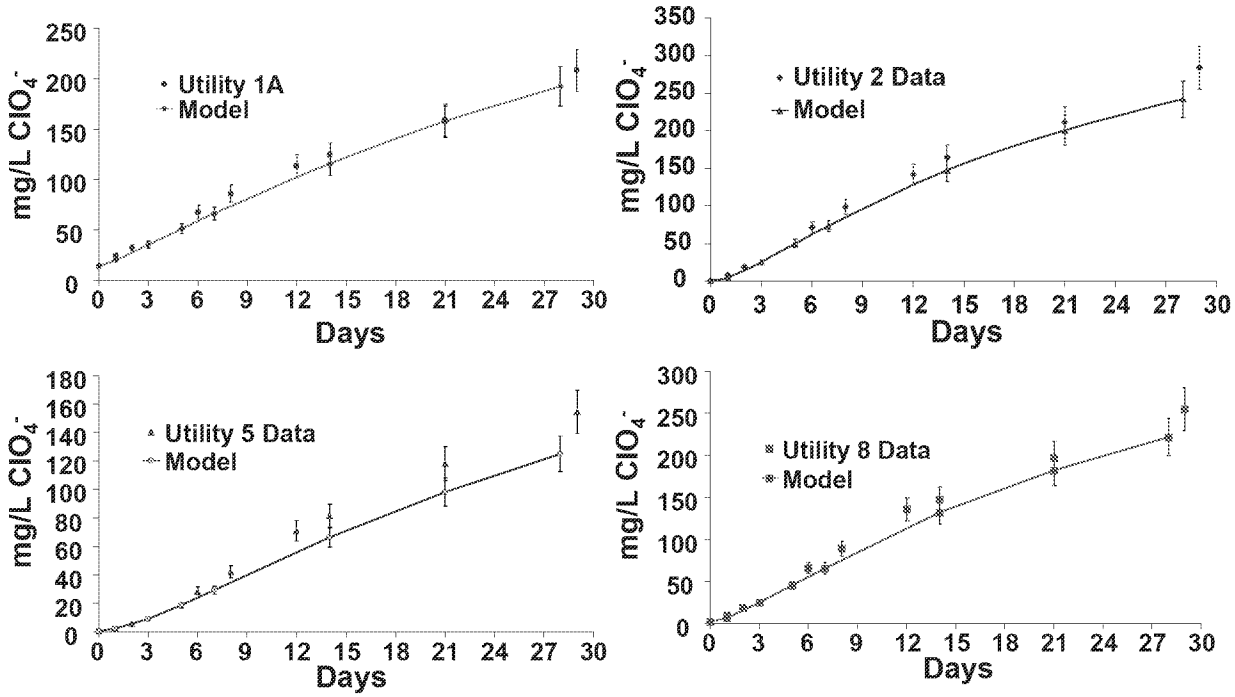

Figure 5.7 Measured vs. predicted concentrations of ClO_4^- in hypochlorite using the Predictive Model: Utility 1, 2, 5, and 8 aged at 50 °C; Error bars are +/- 10%

Finally, in a demonstration of the importance of the "master variables" (ionic strength and concentration of chlorate and hypochlorite), the observed rate of perchlorate formation in each of the bulk hypochlorite, OSG, and calcium hypochlorite was plotted against ionic strength (Figure 5.8) and the molar product (Figure 5.9). Table 5.13 lists the observed rate and rate constants for the OSG and calcium hypochlorite solutions. While the correlation was reasonable for the constant molar product, a significant amount of variability was introduced with the OSG solutions, likely a function of their low pH range (pH 8.8 to 9.8). When the OSG samples are removed (Figures 5.10 and 5.11), a much better correlation (as reflected by the R^2 values) is observed between the observed rate and ionic strength and the observed rate and molar product. The remaining variability in the ionic strength plot (Figure 5.11) may be explained by the use of a surrogate for ionic strength (i.e., conductivity) rather than the true ionic strength of the solution.

Table 5.13
Observed rate and rate constants of perchlorate formation in OSG hypochlorite and calcium hypochlorite solutions

	I (mol/L)	pH	[OCl-] (mol/L)	[ClO3-] (mol/L)	Observed *Rate ($\times 10^{-9}$)	**k_{obs} ($\times 10^{-6}$)
OSG 1a	0.669	9.36	0.137	0.0016	68	300
OSG 1b	0.589	9.26	0.113	0.0029	47	140
OSG 2a	0.945	9.12	0.096	0.0012	45	410
OSG 2b	0.526	9.23	0.097	0.0043	46	110
OSG 3	0.682	9.28	0.144	0.0032	95	200
OSG 4	0.502	8.77	0.064	0.0139	22	25
OSG 5	1.15	9.06	0.113	0.0031	72	200
OSG 6	0.546	9.41	0.073	0.0021	15	96
OSG 7	0.923	9.47	0.101	0.0070	82	120
OSG 8a	0.280	9.28	0.052	0.0024	31	250
OSG 8b	0.250	9.84	0.049	0.0020	22	220
OSG 9	0.828	9.38	0.096	0.0057	140	260
OSG 10	0.882	9.36	0.123	0.0045	94	170
CalHypo1 @ 50 °C	0.748	11.2	0.446	0.0047	389	187
CalHypo2 @ 50 °C	1.38	11.5	0.859	0.0099	2700	319
CalHypo1 @ 60 °C	0.748	11.4	0.443	0.0052	540	235
CalHypo2 @ 60 °C	1.38	11.5	0.874	0.0099	3500	409

*Rate in units of mol ClO_4^- / L / d;
**k in units of L / mol ClO_4^- / d

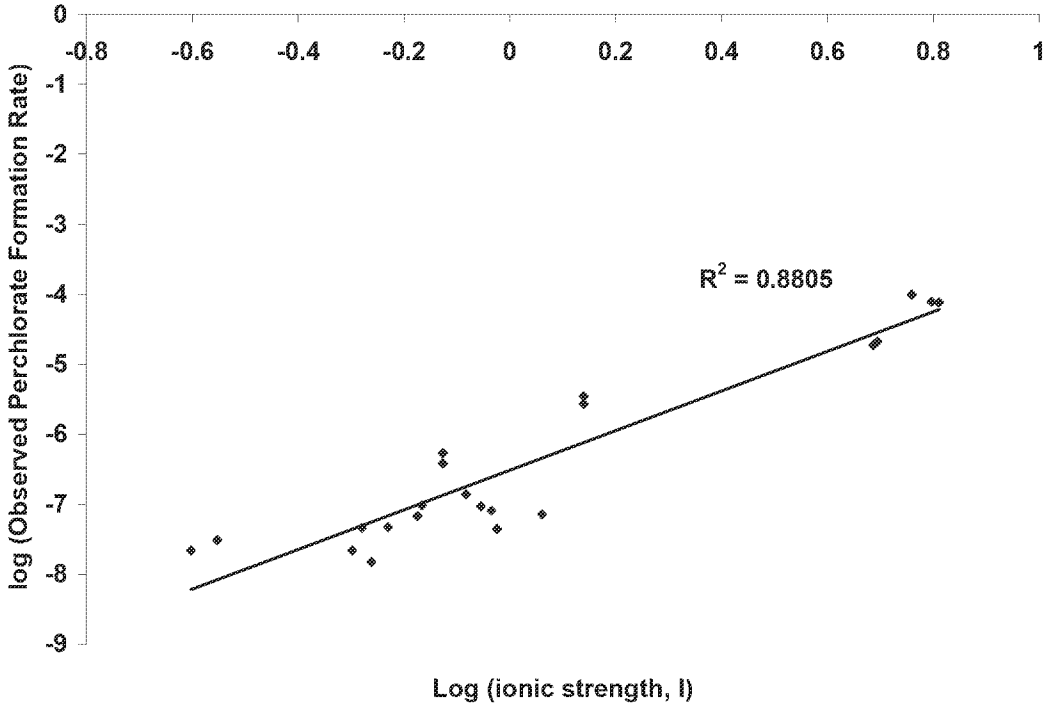

Figure 5.8 Relationship between observed rate of perchlorate formation and ionic strength for bulk, OSG, and calcium hypochlorite samples

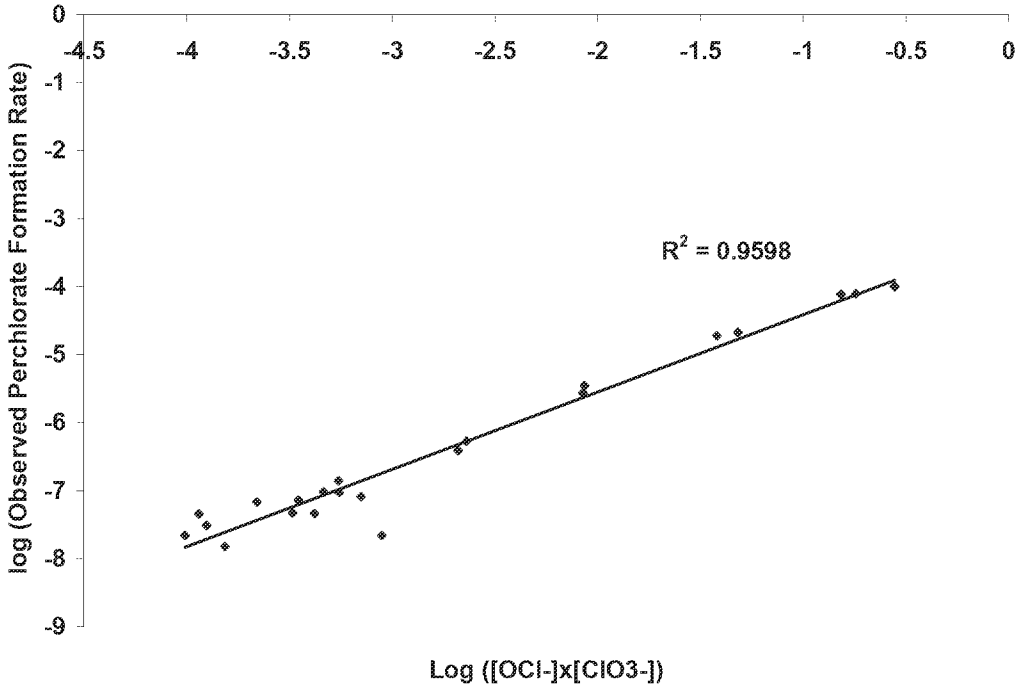

Figure 5.9 Relationship between observed rate of perchlorate formation and the molar product of hypochlorite and chlorate for bulk, OSG, and calcium hypochlorite samples

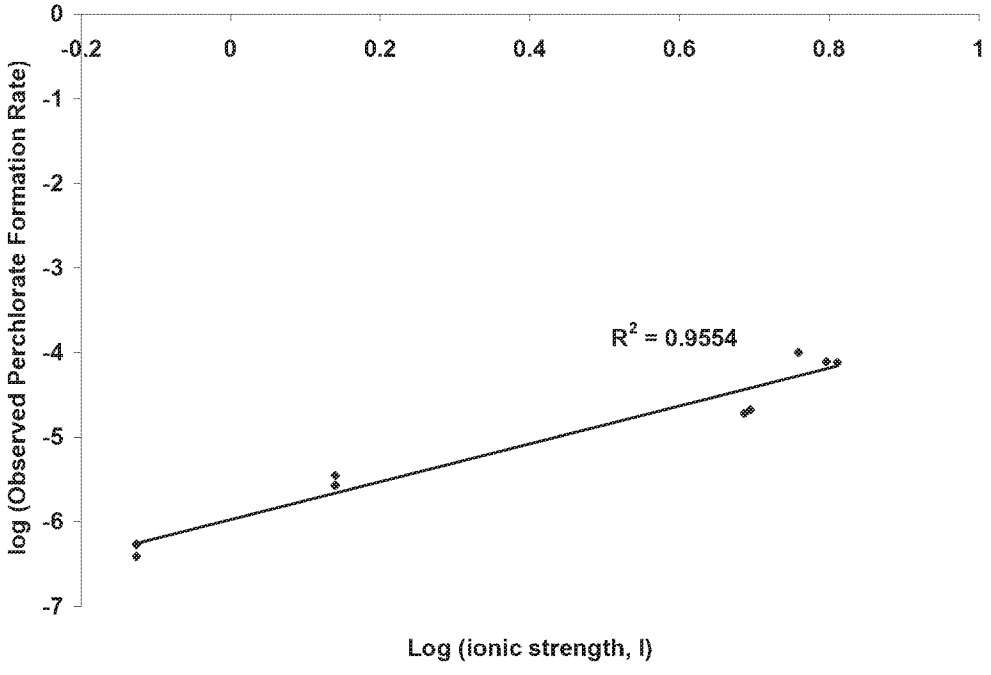

Figure 5.10 Relationship between observed rate of perchlorate formation and ionic strength for bulk and calcium hypochlorite samples only

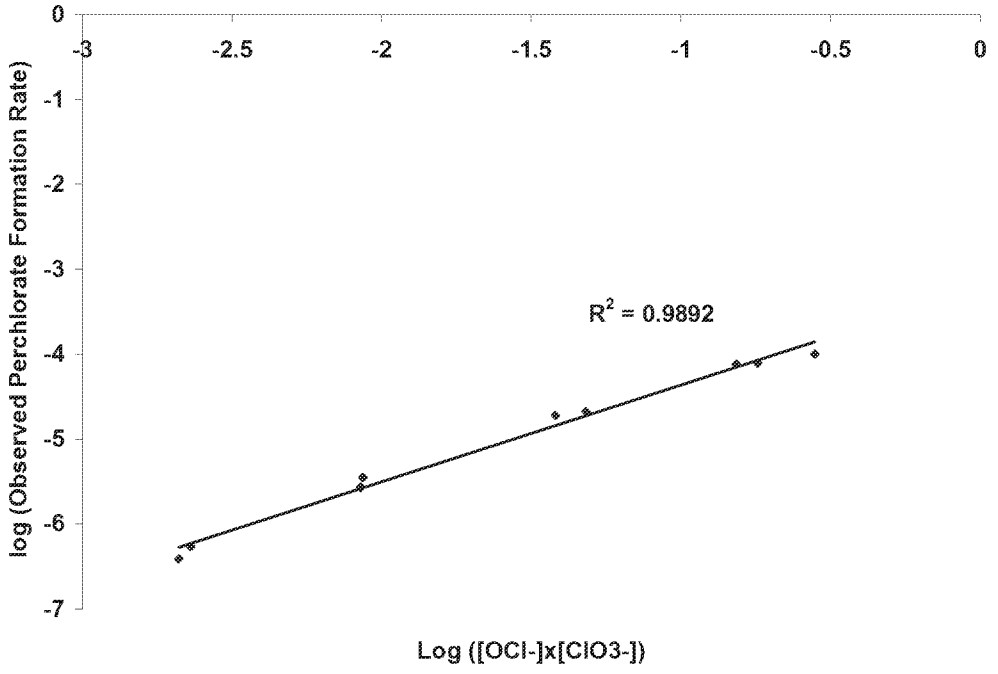

Figure 5.11 Relationship between observed rate of perchlorate formation and the molar product of hypochlorite and chlorate for bulk and calcium hypochlorite samples only

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SUMMARY

In summary, the detailed chemical rate law (i.e., "Predictive Model") can be applied to bulk sodium hypochlorite solutions in conjunction with *Bleach 2001* to predict perchlorate formation over time at various temperatures and ionic strength. The model is only applicable to bulk sodium hypochlorite in pH 11-13 range due to the design of *Bleach 2001* working only within the specifications for bulk hypochlorite solutions. At the high temperature selected for aging the bulk hypochlorite samples (50 °C), the "Predictive Model" was able in 3 out of 4 cases to predict actual perchlorate concentrations within 10% of the measured value. Furthermore, observed rates of perchlorate formation in bulk hypochlorite and calcium hypochlorite solutions correlated well with ionic strength and the molar product of hypochlorite and chlorate.

The errors in correlation and prediction observed could be due to the use of a surrogate (i.e., conductivity) for ionic strength instead of true ionic strength. The only way to determine the "true" ionic strength would be to measure the concentration of each cation and anion in the solution and then sum their individual concentrations into a combined ionic molarity. Such an undertaking would be impractical at best for an individual utility wanting to estimate what impact different storage scenarios would have on perchlorate formation. Thus, in bulk hypochlorite solutions that vary widely in quality and starting concentration of each contaminant, using conductivity as a surrogate provides an appropriate and useful surrogate for ionic strength. Furthermore, the model has demonstrated its ability to predict the *trends* of perchlorate formation which, from a utility perspective, is the most useful information to guide the decision making about how best to store bulk hypochlorite solutions.

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Adam, Luke, Gilbert Gordon, and Don Pierce. 2001. *Bleach 2001*. Miami University, Oxford, Ohio. Copyright (c) 2001 AwwaRF and AWWA.

Asami, M., K. Kosaka, and S. Kunikane. 2007. Bromate, Chlorate, Chlorite, and Perchlorate in Sodium Hypochlorite Solution Used for Water Supply. *Asian Pacific Regional Exhibition, International Water Association*:10-14.

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Gordon, Gilbert, Luke C. Adam, Bernard P. Bubnis, Ching Kuo, Robert S. Cushing, and Richard H. Sakaji. 1997. Predicting Liquid Bleach Decomposition. *Journal American Water Works Association*, 89 **(4)**:142-149.

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Greiner, Peter, Clif McLellan, Dale Bennett, and Angie Ewing. 2008. Occurrence of Perchlorate in Sodium Hypochlorite. *American Water Works Association Journal*, 100 **(11)**:68-74,10.

Howd, Robert H. 2002. Memorandum: Proposed Action Level for Chlorate. CA Office of Environmental Health Hazard Assessment. Sacramento, CA. http://oehha.ca.gov/water/pals/chlorate.html

Kosaka, Koji, Mari Asami, Yukiko Matsuoka, Masahiro Kamoshita, Shoichi Kunikane. 2007. Occurrence of Perchlorate in Drinking Water Sources of Metropolitan Area in Japan. *Water Research*, 41:3474 – 3482.

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CHAPTER 6
CONCLUSIONS AND SUMMARY

DISCUSSION

In the first part of this study, two methods were validated for the analysis of perchlorate and chlorate in hypochlorite solutions: titration and LC-MS/MS. The titration method was better suited for use with concentrated (>5% FAC) hypochlorite solutions while the LC-MS/MS method was better suited for use with lower concentration (<5%) hypochlorite and water samples. Bromate was quantified using LC-MS/MS and transition metals were quantified using ICP-MS. Malonic acid was found to be the most reliable and appropriate quenching agent for use in the study, providing no measurable interference in analysis, no problems associated with storage, and no major safety issues associated with shipping, handling, and the quenching reaction itself.

The methods developed in the early stages of the study were used to investigate factors impacting the rate of formation of perchlorate and bromate in hypochlorite solutions. Bromate was found to form within one to two days of introduction of bromide into hypochlorite solutions. Furthermore, bulk hypochlorite and OSG samples received from utilities showed little-to-no additional bromate formation. Thus, the data suggest that nearly all bromate is formed during manufacture or shortly thereafter. Perchlorate formation, on the other hand, was slow enough to measure and was impacted by several sets of factors: (1) Direct (mechanistic) factors including hypochlorite ion concentration, chlorate ion concentration, and ionic strength. (2) Indirect factors including the presence of metal ions and the presence of bromide ion. (3) Environmental factors including pH and temperature. While it is possible to argue that pH is really a mechanistic factor and that ionic strength is really an environmental factor, their effects were categorized as such to simplify discussion of the detailed chemical rate law. Bromide and metal ions were found to impact the formation of perchlorate indirectly by enhancing the loss of hypochlorite, either through decomposition (catalyzed by metals) or formation of bromate. The effect of pH was important, but in the pH 11 – 13 range was not shown to be a major factor in perchlorate formation.

After separating the factors impacting the rate of perchlorate formation, a detailed chemical rate law describing the dependence of perchlorate formation on ionic strength, hypochlorite ion concentration, chlorate ion concentration, and temperature was developed. While initial data indicated the rate of perchlorate formation may have been greater than second order and a result of parallel or consecutive mechanisms, ionic strength turned out to be the "master variable" controlling the reaction rate. As such, the formation of perchlorate is first order in hypochlorite and chlorate ion concentration and is highly dependent upon ionic strength and temperature. Thus, the detailed chemical rate law was used as a "Predictive Model" to predict perchlorate concentration to within 10% of the measured perchlorate concentration in multiple bulk hypochlorite samples aged at different temperatures for up to 200 days. Furthermore, the "Predictive Model" was then used to develop a set of quantitative recommendations for utilities to use to minimize the amount of perchlorate formation in stored bulk hypochlorite solutions. It should be noted, however, that given the time limitation of the study, the model was not validated on real samples below 30 °C. Thus, any predictions below 30 °C should be limited to a qualitative assessment of how dilution and temperature changes impact

perchlorate formation rather than an exact prediction of the actual concentration of perchlorate expected.

Finally, a set of 5 bulk hypochlorite solutions, 12 OSG hypochlorite solutions, and one calcium hypochlorite sample was obtained for contaminant analysis and quantification and was used in a holding study to examine the rate of perchlorate formation in each solution. All samples tested had measurable concentrations of chlorate, perchlorate, and bromate. No specific conclusions could be made regarding differences in contaminant concentrations in bulk, OSG, and calcium hypochlorite solutions. There did appear to be, however, a link between salt quality and bromate concentration in OSG samples, suggesting that a salt of a higher purity (in this study, >99.5% as NaCl) may be useful for reducing the amount of bromate in the hypochlorite product. However, this trend needs to be further investigated before a specific recommendation on salt purity and maximum levels of bromide can be quantified. When the various solutions were aged, good correlation was observed between the rate of perchlorate formation, the concentration of hypochlorite and chlorate ions, and ionic strength. Furthermore, the "Predictive Model" was able to predict perchlorate formation in the commercial bulk hypochlorite samples to within 20% of the measured concentration for up to 28 days at 50 °C.

RECOMMENDATIONS

Based on the findings presented in this report, several key factors have been identified that impact the formation of perchlorate, bromate, and other contaminants in hypochlorite solutions. The major factors impacting perchlorate formation parallel those previously described for reducing the decomposition of hypochlorite: temperature, ionic strength, concentration, and pH. By using the information gathered during this study and by applying the "Predictive Model" to hypothetical liquid hypochlorite storage scenarios, several quantitative and qualitative recommendations can be made:

a. Dilute stored hypochlorite solutions upon delivery: The decomposition of hypochlorite and subsequent formation of chlorate and perchlorate is dependent upon hypochlorite concentration and ionic strength. Higher ionic strength and hypochlorite concentration will drive the reaction towards a greater production of chlorate and perchlorate while also increasing the rate of decomposition of hypochlorite. By diluting a 2 molar hypochlorite solution by a factor of 2, the rate of perchlorate formation decreases by a factor of 7 due to the combination of concentration and ionic strength effects A four-fold dilution of a hypochlorite solution will decrease the rate of formation by 36. A ten-fold dilution of a hypochlorite solution will decrease the rate of perchlorate formation by a factor of 270.

b. Store the hypochlorite solutions at lower temperatures: Higher temperatures speed up the chemical decomposition of hypochlorite and the subsequent formation of chlorate and perchlorate. Every 5 °C reduction in storage temperature will reduce the rate of perchlorate formation by a factor of approximately 2.

c. Control the pH of stored hypochlorite solutions at pH 11 – 13, even after dilution: Storage of concentrated hypochlorite solutions at pH values lower than 11 is not recommended due to rapid decomposition of hypochlorite ion/hypochlorous acid and the consequent formation of chlorate even though this reduces the amount of

perchlorate formed. When the pH is higher than 13, perchlorate formation is enhanced due to the ionic strength effect. As such, utilities should continue to insist that manufacturer specifications include pH control in the range of 11 to 13. Given the typical pH range of OSG hypochlorite (pH 9 to 10), such solutions should be used as soon as possible after manufacture and should not be stored for more than 1-2 days.

d. Control the removal of transition metal ions by purchasing filtered hypochlorite solutions and by using low-metal ion concentration feed water for the OSG systems: The presence of transition metal ions results in an increased degradation rate of hypochlorite. While this degradation is concomitant with reduced perchlorate formation, the FAC concentration is also reduced, forcing a utility to use a higher volume of a hypochlorite solution which results in higher mass loading of contaminants such as perchlorate, chlorate, and bromate.

e. Use fresh hypochlorite solutions when possible: Over time, hypochlorite will naturally decompose to produce oxygen, chlorate, and perchlorate. Less storage time will minimize the formation of these contaminants in the hypochlorite solution. A fresh hypochlorite solution will also contain a higher concentration of hypochlorite, thereby reducing the amount of solution required to obtain the target chlorine residual. Again, higher hypochlorite concentration in a fresh hypochlorite solution will correspond to lower concentrations of contaminants dosed.

f. For utilities using OSG hypochlorite, use a low-bromide salt to minimize the amount of bromide present in the brine: Bromate formation will occur rapidly in hypochlorite solutions in the presence of bromide. By controlling the amount of bromide in the salt and source water used for on-site generation, bromate formation can be minimized.

If a utility were to combine dilution with temperature reduction, a significant impact on hypochlorite decomposition and perchlorate formation would be observed. For example, as described in Chapter 4 if a utility were to dilute a 13% bulk hypochlorite solution by a factor of 2 and also reduce the storage temperature by 10 °C, the result would be 16 times less hypochlorite decomposition and 27 times less perchlorate formation than if the hypochlorite were stored at ambient temperatures undiluted.

Another interpretation of the results of this study is through seasonal trends. If, for example, a utility experienced average bulk hypochlorite storage temperatures of 10 °C in the winter and 35 °C in the summer, the rate of perchlorate formation for 13% hypochlorite would be nearly 18 times faster in the summer. In other words, in winter that utility could expect the concentration of perchlorate concentration to increase by a factor of 10 in approximately 3 months; in summer it would increase by a factor of 10 in only 5 days. Had the hypochlorite solution been diluted by a factor of 2, the same increase in perchlorate concentration would take one month in summer and 20 months (assuming, for example, an average temperature of 10 °C) in winter. Therefore, in order to minimize the amount of perchlorate formation in hypochlorite solutions, a combination of dilution and temperature control is recommended.

FUTURE WORK

While the "Predictive Model" is appropriate for use in bulk hypochlorite solutions, it would be interesting to build in a pH dependence to assist with predictions for OSG hypochlorite which may have pH values in the range of 9 to 10. Also, according to Adam and Gordon (1999), some chloride ion-specific dependence exists within the mechanism of chlorate formation. The direct impact of chloride ion formation (other than in its use to increase ionic strength) was not investigated. Thus, future studies examining the impact of chloride ion on perchlorate formation may be investigated. Furthermore, ionic strength was measured by a surrogate, conductivity, and thus does not reflect the "true" ionic strength of the solution. The detailed chemical rate law incorporates the measured "ionic strength", but may benefit from the incorporation of the "true" ionic strength. As such, future studies are also recommended which may address this issue. The relationship between salt purity and bromate formation during OSG production of hypochlorite needs to be quantified and should be investigated more thoroughly. Finally, in order to assess the behavior of chlorate, perchlorate, and bromate in distribution systems an in-depth study with more sampling sites (and distribution systems) combined with temporal observations over a period of several months is suggested as a future research direction. Such information may indicate whether any contaminant violations could occur in distribution systems with high temperatures and long residence times.

REFERENCES

Adam, Luke C. and Gilbert Gordon. 1999. Hypochlorite Ion Decomposition: Effects of Temperature, Ionic Strength, and Chloride Ion. *Inorganic Chemistry*, 38 **(6)**:1299-1304.

LIST OF ABBREVIATIONS

Abbreviation	Description
$\Delta H^{\ddagger}$	Enthalpy of Activation
$\Delta S^{\ddagger}$	Entropy of Activation
ACS	American Chemical Society
ARDC	Applied Research and Development Center
AWWA	American Water Works Association
CA DPH	California Department of Public Health
DNA	Deoxyribonucleic Acid
DSA	Dimensionally Stabilized Anode
DWEL	Drinking Water Equivalent Level
DWTP	Drinking Water Treatment Plant
EPA	*See US EPA*
FAC	Free Available Chlorine
GW	Groundwater
HDPE	High Density Polyethylene
I	Ionic Strength
IC-CD	Ion Chromatography with Conductivity Detection
IC-MS/MS	Ion Chromatography with Tandem Mass Spectrometry
IC-PCR	Ion Chromatography with Post Column Reaction
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
JNIPH	Japanese National Institute of Public Health
k_0	Rate Constant at Zero Ionic Strength
k_2	Hypothetical Second Order Rate Constant
k_b	Boltzmann's Constant
k_{calc}	Calculated Rate Constant
k_{obs}	Observed Rate Constant
LC-MS	Liquid Chromatography with Mass Spectrometry
LC-MS/MS	Liquid Chromatography with Tandem Mass Spectrometry
M	Molarity (mol/L)
MA DEP	Massachusetts Department of Environmental Protection
MCL	Maximum Contaminant Level
MP	Molar Product
MRL	Method Reporting Limit
MS/MS	Tandem Mass Spectrometry

Abbreviation	Description
NOEL	No Observable Effect Level
NSF/ANSI	NSF International/American National Standards Institute
OD	Ocean Desalination
OSG	On-Site Generator
PAC	Project Advisory Committee
PPD	Pounds Per Day
R	Ideal Gas Law Constant
R^2	Pearson Correlation Coefficient Squared
RfD	Reference Dose
RFP	Request for Proposals
RSD	Relative Standard Deviation
SDS	Simulated Distribution System
SNWA	Southern Nevada Water Authority
SPE	Solid Phase Extraction
SW	Surface Water
t	Time
T	Temperature
TDS	Total Dissolved Solids
THMs	Trihalomethanes
US	United States
US EPA	United States Environmental Protection Agency
UV	Ultraviolet Light
v/v	volume/volume
WHO	World Health Organization
WW	Tertiary Treated Wastewater

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 2/24/2020 5:15:46 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: FW: Revised Document
Attachments: Perchlorate Recommendations for PWS 2-21-20.docx; Perchlorate Reductions 2-19-20 v1.docx

Sam –
Here's the CCR response for the comment bubbles in each document.
141.153(d)(3)(ii) UCMR results "need only be included in CCR for 5 years from the date of last sample or until any of the contaminants becomes regulated and subject to routine monitoring requirements, whichever comes first." (Most CWSs do not maintain past years CCR on their web site).

Lisa

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, February 24, 2020 11:38 AM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Subject: FW: Revised Document

From: McLain, Jennifer L.
Sent: Sunday, February 23, 2020 9:13 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: Revised Document

Thank you Eric & Lisa – The attached contain a very few edits/comments. And then, these are ready to go to OW for review. Regarding the outreach plan, continue to pursue the discussions with ASDWA and AWWA as we discussed and agreed to with Dave. However, I'm not sure that we can say these reports will be released soon, maybe it is better to say that there is the potential for them to be issued in the near term.

Thanks much,
Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Friday, February 21, 2020 10:15 AM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Subject: FW: Revised Document

Jennifer: We have updated the recommendations document to reflect the comments you provided earlier. Attached also is a plan to contact States and AWWA next week to verify our information and discuss with the states what assistance might be provided.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: Burneson, Eric
Sent: Thursday, February 20, 2020 4:19 PM
To: McLain, Jennifer L. <Mclain.Jennifer@epa.gov>
Cc: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>; Christ, Lisa (Christ.Lisa@epa.gov) <Christ.Lisa@epa.gov>
Subject: RE: Revised Document

Jennifer;
Attached please find revised perchlorate documents. We have revised the perchlorate reductions document with a view towards public release. We have also prepared the attached plan to work next week with ASDWA and AWWA to verify information about the systems and prepare states to assist systems.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: McLain, Jennifer L.
Sent: Wednesday, February 12, 2020 11:24 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>
Subject: RE: Revised Document

Eric – would you please review this document with an eye towards the future public version. Once you have a chance to talk to the team, I would appreciate a plan for stakeholder engagement/outreach.

Thanks
Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Wednesday, February 12, 2020 9:53 AM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Subject: FW: Revised Document

Attached is the update on systems and perchlorate reductions. The only outstanding system is in LA.

From: Christ, Lisa
Sent: Wednesday, February 12, 2020 9:50 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: FW: Revised Document

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, February 10, 2020 12:37 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Revised Document

Hi Lisa,

We got new information from the MD system. There was some misunderstanding with the information request but here is the latest.

The treatment plant at chapel hill was recently taken off line and it was replaced with new productions wells and treatment plant which started operations in January 27, 2020. Please see the new language that I have incorporated in the revised document below.

"EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that the Chapel Hill WFP was taken off line and it was replaced with a new treatment plant and five new production wells. The new treatment plant started operations on January 27, 2020. System personnel also indicated that monitoring was conducted in November 2019 and the analysis shows that perchlorate was not detected in either the source well water or the finished water."

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Monday, February 10, 2020 10:31 AM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>

Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Revised Document

Thanks Sam.
Do we know exactly what the contractor asked each PWS? Based on this response: **EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that no follow-up/updated monitoring data for perchlorate is available.** It appears we only asked about monitoring…did the contractor ask about any changes in source water and/or treatment too?

Thanks,
Lisa

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, February 10, 2020 8:14 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: Revised Document

Hi Lisa,

We heard back from the Chapel Hill system in MD and they do not have new data for Perchlorate. The document has been updated accordingly. Please see attached.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 11/20/2019 3:22:10 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
CC: Huff, Lisa [Huff.Lisa@epa.gov]
Subject: RE: Perchlorate briefing
Attachments: Option Selection for Perchlorate 11-19-19 v2.docx

Hi Sam,
The briefing looks good. I had just a couple edits. Did you share the draft with Jamie and Greg? Has OGC signed off on this draft? Has a meeting request with Dave been submitted?

Thanks,
Lisa

-----Original Message-----
From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Tuesday, November 19, 2019 9:43 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: RE: Perchlorate briefing

Hi Eric,

I have incorporated your edits as well as the additional occurrence data provided by the Reg Det Team, and the new input from OGC.

Please take particular attention to the edits I made to the language you inserted in the "Rationale" section of Option 1. I made the edits considering the data provided by the Reg Det Team.

Let me know if you have any comments.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

-----Original Message-----
From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Friday, November 15, 2019 2:16 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: RE: Perchlorate briefing

Sam I just sent you my comments on the previous version. Let me know if there are edits you made in your version that need to be incorporated into mine.

-----Original Message-----
From: Hernandez-Quinones, Samuel
Sent: Friday, November 15, 2019 2:07 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: RE: Perchlorate briefing

Hi Eric,

I have updated the briefing document after talking with Lisa Huff about the additional edits you wanted to see in the document.

if you would like us to include any additional information.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

-----Original Message-----
From: Huff, Lisa <Huff.Lisa@epa.gov>
Sent: Thursday, November 14, 2019 4:32 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>
Subject: Re: Perchlorate briefing

Thanks Sam. Looks like you have the relevant points other than Eric said we should put as an option the MCLG if 18 not the other values. I'll talk to you in the morning and we can see what Eric wants to see.

Lisa

> On Nov 14, 2019, at 3:51 PM, Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov> wrote:
>
> Hi Lisa,
>
> I sent a revised draft version of the briefing document to Eric earlier this week. We are waiting for additional input that OGC will provide to us. Here is the revised document, as reviewed by Lisa, that I shared with Eric. If you have additional information, I will be glad to incorporate into the document.
>
> I will be in the office tomorrow morning if you want to hand those notes to me, or you can also email them.
>
> Thanks
> Sam
> ==========
> Samuel Hernández Quiñones, P.E.
> Environmental Engineer
> Office of Water
> Environmental Protection Agency
> 1200 Pennsylvania Ave. NW
> Washington, DC 20460
> 202-564-1735
>
> "USEPA Protecting Human Health and the Environment"
>
> -----Original Message-----
> From: Huff, Lisa <Huff.Lisa@epa.gov>
> Sent: Thursday, November 14, 2019 3:37 PM
> To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
> Cc: Christ, Lisa <Christ.Lisa@epa.gov>
> Subject: Perchlorate briefing
>
> Sam,
> I just had a conversation with Eric. He said the meeting with with Dave Ross and the Administrator has been delayed however he said we need to put together the briefing materials ASAP. He gave me a brief summary of the 3 options to reflect based on direction from last week. I can email you those point but thought you might have in your notes. He had one addition that is for the option recommending a MCL we should specify that value would be 18. Have you been working on preparing materials? Eric was hoping to have them by tomorrow for his review. Please let me know. I'm out of the office for an appt. but will follow up via email shortly.
>
> Lisa
> <Option Selection for Perchlorate 11-12-19 v1.docx>

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 11/8/2019 6:39:28 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: RE: Revised Briefing Document
Attachments: Option Selection for Perchlorate 11-8-19 v2.docx

Hi Sam,
I did some rewording, but want to make sure this is still accurate. Please take a look and make changes as needed.

Thanks,
Lisa

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Friday, November 08, 2019 1:00 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: Revised Briefing Document

Hi Lisa,

Here is the revised document. The edits are highlighted. Let me know if you have any comments or edits.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 12/12/2019 10:10:33 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
CC: Khera, Rajiv [khera.rajiv@epa.gov]; Huff, Lisa [Huff.Lisa@epa.gov]
Subject: FW: Perchlorate Briefing Document
Attachments: Redline-Responses - Option Selection for Perchlorate 11-21-19 v1 jlmkw.docx; Clean Version - Option Selection for Perchlorate 12-2-19 v1.docx

Hi Sam,
We need to develop a couple additional options.
1. Dave has suggested for water systems to "spring into" monitoring versus monitor to go to reduced/waivers. Work with the team to come up with your best professional judgement as to how many systems would be require to monitor for perchlorate by states. We'll need to come up with criteria for when we believe a state would require monitoring (e.g., water system is close to a facility that produces/uses perchlorate, has previous monitoring at levels close to the proposed MCL, uses hypochlorate, etc). Lisa Daniels of PA stated during NDWAC that she wouldn't offer any water systems who use hypochlorate to get a waiver, so we'll need to make some assumptions about how different states would implement. Some states by law cannot be more stringent than federal regulations, so we'll need to factor that in too. Once you've estimated the number of systems, we'll need to make assumptions about how initial, reduced and monitoring waivers will be implemented (maybe the same as proposed?). Also, we'll need a new cost/benefit estimate for this option. Please utilize your team members to help with this.
- ask Tom to research what is known about the levels of perchlorate in finished water due to hypochlorate use vs. perchlorate in source water.
-have other team members do some digging into SDWIS data to see if that helps inform this option.
-have a team member see if facilities that use/produce perchlorate can be identified to help estimate water systems within a certain proximity.

2. Assume all surface water systems will take 4 quarters of initial monitoring and all groundwater systems will take two quarters of initial monitoring and then if below the MCL will go directly to 9 year reduced monitoring (not a waiver). This cost/benefit estimate will also need to be done.

I'm out tomorrow and Monday, but would like to meet Tuesday to go over materials. The above options can be on a separate document for now. Eric wants a draft net week! We won't be able to get to option selection until we've explored Dave's suggestion and alternative 2 above.

If you have any questions, give me a call Ex. 6 Personal Privacy (PP)
I know this is a real challenge! Thanks,
Lisa

Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, December 02, 2019 4:36 PM
To: Mclain, Jennifer <Mclain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: Perchlorate Briefing Document

Jennifer

Attached are a clean and redline copy of the perchlorate briefing document with your edits incorporated and your comments/questions addressed. If you are comfortable with the attached I recommend you transmit the clean version to OW and that we bring a copy to OLEM for our discussion tomorrow.

Eric

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 5/19/2020 10:31:07 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: RE: Draft Perchlorate Response to Comment Document
Attachments: Consolidated Perchlorate Draft Comment Response Document 5-19-20 v2-track change.docx

Hi Sam,
Thanks for your work on this. I did make some modifications, I think there my have been some miscommunication on the use of the summary responses at the start of each chapter, so I made a few adjustments. I also shortened the introduction. I'm sending a clean version of the attached to Jennifer for review.

Lisa

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Tuesday, May 19, 2020 2:06 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: Draft Perchlorate Response to Comment Document

Hi Lisa,

Attached are the redline and clean versions of the draft Perchlorate RtC Document. These incorporate all the suggested edits we have received so far from Eric, OGC, Team Members and others.

Let me know if you have any questions.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 1/23/2020 3:20:24 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: FW: SRMD/HECD Coordination
Attachments: Draft Perchlorate Compendium.docx; PERCHLORATE - SRMD&HECD.v2.docx

FYI --

From: Christ, Lisa
Sent: Wednesday, January 15, 2020 12:35 PM
To: Bradford, Charlotte <Bradford.Charlotte@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Behl, Betsy <Behl.Betsy@epa.gov>; Flaherty, Colleen <Flaherty.Colleen@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>; Wang, Lili <Wang.Lili@epa.gov>; Hautman, Dan <Hautman.Dan@epa.gov>; Carroll, Gregory <Carroll.Gregory@epa.gov>; Albert, Ryan <Albert.Ryan@epa.gov>; Strong, Jamie <Strong.Jamie@epa.gov>
Cc: Reiley, Mary <Reiley.Mary@epa.gov>; Greene, Sophie <greene.sophie@epa.gov>; Miller, Gregory <Miller.Gregory@epa.gov>; Forrest, Kesha <Forrest.Kesha@epa.gov>
Subject: RE: SRMD/HECD Coordination

DRAFT -- INTERNAL DELIBERATIVE

All,
Attached is the current schedule for the tentative decision by Administrator Wheeler to withdraw the reg det. I've also attached the compendium of public comments. For the withdraw option, we can limit the scope of public comment topics we need to address. We are confirming this with OGC since our attorney has changed. We believe the topics we'll need to respond to include: withdrawing the reg det; the interim health advisory; health effects; and SDWA authority. I've highlighted the topics where we'll need OST support.
Lisa

-----Original Appointment-----
From: Bradford, Charlotte <Bradford.Charlotte@epa.gov>
Sent: Thursday, October 03, 2019 11:16 AM
To: Bradford, Charlotte; Burneson, Eric; Behl, Betsy; Flaherty, Colleen; Rodgers-Jenkins, Crystal; Huff, Lisa; Wang, Lili; Hautman, Dan; Carroll, Gregory; Albert, Ryan; Christ, Lisa; Strong, Jamie
Cc: Reiley, Mary; Greene, Sophie; Miller, Gregory; Forrest, Kesha
Subject: SRMD/HECD Coordination
When: Wednesday, January 15, 2020 3:00 PM-4:00 PM (UTC-05:00) Eastern Time (US & Canada).
Where: DCRoomEast2339/DC-ICC-OW-OGWDW

CONFERENCE CALL-IN Ex. 6 Personal Privacy (PP) **CODE:** Ex. 6 Personal Privacy (PP)

AGENDA

- CCL5 Update
- Perchlorate NPDWR—FY 20 Plan

- Schedule
- Inputs and Deliverables needed from HECD

Please identify any other topics to be covered.

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 1/22/2020 4:08:08 PM
To: Miller, Gregory [Miller.Gregory@epa.gov]
CC: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: FW: FOR REVIEW: Perchlorate Reductions Over Time
Attachments: Reductions of Perchlorate in Drinking Water 1-22-20 .docx

Greg – FYI only. We'll make sure you have the final version of this and the other document.

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Wednesday, January 22, 2020 11:02 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Subject: RE: FOR REVIEW: Perchlorate Reductions Over Time

Lisa:
Thank you and the team for the great work in preparing this document. I have some comments and edits in the attached. Please let me know if you have any concerns or questions.
Eric

From: Christ, Lisa
Sent: Tuesday, January 21, 2020 1:48 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: FOR REVIEW: Perchlorate Reductions Over Time

Eric,
Attached is the document describing reductions in perchlorate since UCMR1. We worked with OPP on the labeling language and with OLEM on the list of superfund sites. Water systems that are being contacted by Abt are highlighted yellow. We're in the process of modifying the PWS recommendations and will have that ready for Jennifer soon.
Let us know if you have questions or concerns.
Lisa

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Friday, January 17, 2020 5:14 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>; Alattar, Zaineb <alattar.zaineb@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Wadlington, Christina <Wadlington.Christina@epa.gov>
Subject: RE: FOR REVIEW: Perchlorate Recommendations for PWS

Lisa and team:
Thank you for the great work to prepare this document so quickly. It is a great. I do have a number of edits and comments but I believe we are heading in the right direction. Please look at my comments in the attached and let me know if you would like to discuss on Tuesday or Wednesday.
The next draft should get input from our Comms director which is why I have copied Christina so that she can start thinking about how she would like to present this information.

Thanks again for the great work.
Eric

From: Christ, Lisa
Sent: Thursday, January 16, 2020 10:05 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>; Alattar, Zaineb <alattar.zaineb@epa.gov>
Subject: FOR REVIEW: Perchlorate Recommendations for PWS

Hi Eric,
Attached is the draft document of recommendations for PWS that may be concerned about perchlorate in drinking water. We are still working on the other document. Let us know if you have questions, etc.

Lisa Christ
Chief, Targeting and Analysis Branch
Office of Ground Water and Drinking Water
202-564-8354

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 2/13/2020 9:46:59 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Khera, Rajiv [khera.rajiv@epa.gov]
Subject: FW: 2 perchlorate documents -- for your records
Attachments: Perchlorate Reductions 2-13-20.docx

Hi Sam & Rajiv,
Attached are Eric's comments on the reductions document. He did not have comment on the PWS recommendations.
Thanks!
Lisa

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Thursday, February 13, 2020 2:05 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: 2 perchlorate documents -- for your records

Thank You Lisa
I have a few comments/edits on the perchlorate reduction document in the attached.
Eric

From: Christ, Lisa
Sent: Wednesday, February 12, 2020 9:59 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: 2 perchlorate documents -- for your records

Eric – just wanted to put both documents in one place for you. Both have been reviewed by Jennifer and Christina. Lisa

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Wednesday, February 12, 2020 9:53 AM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Subject: FW: Revised Document

Attached is the update on systems and perchlorate reductions. The only outstanding system is in LA.

From: Christ, Lisa
Sent: Wednesday, February 12, 2020 9:50 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: FW: Revised Document

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, February 10, 2020 12:37 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>

Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Revised Document

Hi Lisa,

We got new information from the MD system. There was some misunderstanding with the information request but here is the latest.

The treatment plant at chapel hill was recently taken off line and it was replaced with new productions wells and treatment plant which started operations in January 27, 2020. Please see the new language that I have incorporated in the revised document below.

"EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that the Chapel Hill WFP was taken off line and it was replaced with a new treatment plant and five new production wells. The new treatment plant started operations on January 27, 2020. System personnel also indicated that monitoring was conducted in November 2019 and the analysis shows that perchlorate was not detected in either the source well water or the finished water."

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Monday, February 10, 2020 10:31 AM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: RE: Revised Document

Thanks Sam.
Do we know exactly what the contractor asked each PWS? Based on this response: **EPA contacted the Chapel Hill System in January 2020. Water system personnel indicated that no follow-up/updated monitoring data for perchlorate is available.** It appears we only asked about monitoring…did the contractor ask about any changes in source water and/or treatment too?

Thanks,
Lisa

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, February 10, 2020 8:14 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: Revised Document

Hi Lisa,

We heard back from the Chapel Hill system in MD and they do not have new data for Perchlorate. The document has been updated accordingly. Please see attached.

Thanks
Sam

==========

Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 5/19/2020 5:22:27 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: FW: Notice of Final Action on Perchlorate -- Timing for RTC document?
Attachments: Perchlorate Action Memo 5-19-20.docx; Draft Perchlorate Final Action FRN 5-19-20 v1.docx; Transmittal Memo JM to DR 5-18-20.docx

Hi Sam – When will the RTC be ready for Jennifer's review? We need to get that to her as quickly as possible. OW will also need to review before it goes to OMB.
Thanks-
Lisa

From: Christ, Lisa
Sent: Tuesday, May 19, 2020 1:00 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Khera, Rajiv <khera.rajiv@epa.gov>; Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>; Alattar, Zaineb <alattar.zaineb@epa.gov>; Georges, Jessica <Georges.Jessica@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: FW: Notice of Final Action on Perchlorate

FYI only

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Tuesday, May 19, 2020 10:35 AM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Attached is a clean version of the notice with your edits accepted. Also attached is a clean version of the Action memo with the edits I sent you last night accepted. Lastly attached is the unchanged memo from you to Dave Ross.

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Tuesday, May 19, 2020 9:15 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Eric – I have made two minor edits in the attached. I will send this to Charlotte so that she can see how we've addressed her comments. At the same time we will submit formally to OW. Please send us the final clean versions of the memos and the action for that process.

Thanks much
Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, May 18, 2020 8:42 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>

Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Jennifer:
I don't believe a discussion is necessary. Edits and responses to the questions are in the attached. Please let us know if a revised clean version is needed.
Eric

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Monday, May 18, 2020 5:34 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: FW: Notice of Final Action on Perchlorate

Eric – please let me know if you want to discuss.

From: Bertrand, Charlotte <Bertrand.Charlotte@epa.gov>
Sent: Monday, May 18, 2020 5:29 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Braschayko, Kelley <braschayko.kelley@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Aguirre, Janita <Aguirre.Janita@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Thanks – couple of bubble box questions and then I had one redline edit I added to the Notice.

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Monday, May 18, 2020 3:01 PM
To: Bertrand, Charlotte <Bertrand.Charlotte@epa.gov>
Cc: Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Braschayko, Kelley <braschayko.kelley@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Aguirre, Janita <Aguirre.Janita@epa.gov>
Subject: FW: Notice of Final Action on Perchlorate

Charlotte – as agreed, I'm sending you the draft final perchlorate FRN for review. The redline includes the changes made since the FAR. I'm also including the draft Action Memo. Please let us know if your preference is to have these submitted to OW through CMS now or after you have reviewed. Let me know if you want to talk.

Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, May 18, 2020 2:48 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FW: Notice of Final Action on Perchlorate

Jennifer:

Attached for transmission to OW are revised versions of the FRN for the Perchlorate Final Action. There is both a clean and track changes version that includes edits made since initiating FAR (including the edits you asked for on Saturday and adding 3 more SAB recommendations to page 14 that were in the proposal but were not included in the draft we provided you on Friday). Also please find clean version of the transmittal memo from you to Dave Ross and the Action memo incorporating your edits.

Please note that there is also a redline version of the Action Memo for you to see the responses to your comments on the document. I do not recommend transmitting that memo to OW.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, May 18, 2020 2:18 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Hi Eric,

Attached are the revised Redline and Clean versions of the Perchlorate FR Notice. Once we are ready for OP's submittal to OMB let me know and I will provide a version that adheres to OP's file name formatting guidelines.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, May 18, 2020 1:14 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Sam

1. Change the title please. This was requested by OGC at Sr. Leadership levels.
2. Provide the same level of detail on the SAB recommendations as was included in the proposal.
3. I don't think the HRRCA text is necessary and do not want to add it at this stage since there are OGC edits that already make this clear.

Eric

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, May 18, 2020 12:41 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Hi Eric,

Here is a revised Redline of the document (from FAR). We had a few questions/issues for your consideration about the attached file. Specifically:,

1- Page #1, Notice Tittle: We did not accept the edits to the notice tittle. Because, the tittle of the notice was specifically crafted by OGC to capture the multiple actions EPA is taking. Suggest consulting with OGC before modifying this tittle.
2- Page #14, SAB Recommendations: SAB provided 4 main recommendations in 2013 but we only listed the first recommendation. Please advise if we should list all 4 recommendations here or not.
3- Page #26, Missing HRRCA Text: This language was offered by TAB in its 5-13-20 version of the draft FRN, but it did not show up in the version provided by OGWDW with Eric's & Jennifer's comments. We have inserted the language here for the reviewer's consideration. Please advise if we should keep it.

Once you provide your feedback, I will modify the redline version and also provide a Clean copy for transmittal.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, May 18, 2020 8:42 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: FW: Notice of Final Action on Perchlorate

Lisa and Sam
Attached are Jennifer's comments and edits on the draft FRN. I have responded to her questions in the attached and made some additional edits. Can you please get a revised clean version and another redline version that compares this document and the version that was distributed to FAR?
Thanks for your work on this.
Eric

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Saturday, May 16, 2020 11:39 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Looks very good. See p. 6 for my only concern w/the revisions.

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Friday, May 15, 2020 5:03 PM

To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: Notice of Final Action on Perchlorate

Jennifer

Attached for your approval and transmittal to the Office of Water for their approval and transmittal to the Office Policy for initiation of interagency review is a *Federal Register* notice titled: "Notice of Final Action on Perchlorate." Also attached for your review are a draft transmittal memo from you to the Assistant Administrator of Water, a draft Action Memorandum and a track changes version of the FR notice that denotes the changes made as a result of Final Agency Review.

On February 11, 2011, the EPA published a determination to regulate perchlorate in drinking water (76 FR 7762). On June 26, 2019 (84 FR 30524), the EPA published the proposed National Primary Drinking Water Regulation for Perchlorate and requested public comments on multiple alternative actions, including withdrawing the 2011 determination to regulate perchlorate. The EPA received approximately 1,500 comments on the proposed rule. In the attached notice, the EPA is withdrawing the 2011 Regulatory Determination and is making a final determination not to regulate perchlorate based on the Agency's consideration of public comments and the best available information.

I recommend that you approve and transmit the attached notice to the Office of Water for their review, approval and transmission to the Office of Policy to initiate interagency review in accordance with Executive Order 12866. If you need additional information or have questions pertaining to any aspect of this notice, please call me or have your staff contact Samuel Hernandez at 202-564-1735.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 3/22/2017 2:37:47 PM
To: Perkinson, Russ [Perkinson.Russ@epa.gov]
Subject: FW: Perchlorate PR Report
Attachments: Perchlorate Peer Review Report_TO 2015-22_Final.pdf

FYI --

-----Original Message-----
From: Burneson, Eric
Sent: Wednesday, March 22, 2017 10:36 AM
To: Wadlington, Christina <Wadlington.Christina@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Mclain, Jennifer <Mclain.Jennifer@epa.gov>
Subject: FW: Perchlorate PR Report

Christina:
Per our conversation, the attached is the perchlorate peer review report we intend to put into the docket. As discussed a brief desk statement indicating that we are reviewing the recommendations in the report and taking actions to improve the BBDR model is appropriate. We should also note that we intend to undertake peer review of a second document on methodologies to derive a perchlorate MCLG (using the BBDR model).

Eric

-----Original Message-----
From: Christ, Lisa
Sent: Wednesday, March 22, 2017 10:23 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: FW: Perchlorate PR Report

Eric- the peer review report is here and we are ready to post it to the docket. I wanted to check with you first to see if you wanted a briefing or summary of its contents?
There are no surprises in the report, it contains what we heard during the meeting - 1st trimester, TSH feedback, other giotrogens, more uncertainty analysis of key parameters. I've attached the report. If you're interested, in reading the executive summary it's a good representation of the report.

L

-----Original Message-----
From: Jim Rollins [mailto:jerollins@policynavigation.com]
Sent: Wednesday, March 22, 2017 9:51 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Olson, Daniel <Olson.Daniel@epa.gov>; Perkinson, Russ <Perkinson.Russ@epa.gov>
Subject: RE: Perchlorate PR Report

Hi Eric,

Just checking back to see if the report has been posted and to where I should look?

Thanks.

-----Original Message-----
From: Burneson, Eric [mailto:Burneson.Eric@epa.gov]
Sent: Thursday, February 16, 2017 12:59 PM
To: Jim Rollins <jerollins@policynavigation.com>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Olson, Daniel <Olson.Daniel@epa.gov>; Perkinson, Russ <Perkinson.Russ@epa.gov>
Subject: RE: Perchlorate PR Report

Jim: The peer review report has not been posted yet. We expect to post it in early March.

-----Original Message-----
From: Jim Rollins [mailto:jerollins@policynavigation.com]
Sent: Thursday, February 16, 2017 10:00 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: Perchlorate PR Report

Good morning Eric,

Has the peer review report been posted? Where can I find it?

Sent from my iPhone

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 2/6/2020 7:14:24 PM
To: Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]
CC: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Davis, CatherineM [Davis.CatherineM@epa.gov]
Subject: Perchlorate reductions
Attachments: Perchlorate Reductions 2-6-20 v2.docx

Importance: High

Crystal – attached is the 2nd formatted document. There are still PWS that we do not have an update for. Jennifer and I agreed we will need to give states a heads up before this is publicly available. We can use that interaction to request PWS level updates.
Cathy – hold up on calling states for now. Will advise
Many thanks
Lisa

From: Christ, Lisa
Sent: Thursday, February 06, 2020 2:05 PM
To: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: formatted Perchlorate Recommendations for PWS

I spoke with Jennifer and we changed a word in the health effects section.

From: Christ, Lisa
Sent: Thursday, February 06, 2020 9:35 AM
To: Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: formatted Perchlorate Recommendations for PWS

1 of 2 documents.
Crystal,
We formatted the attached and ran it by Christina to get her input. Please see the attached fact sheet.
Christina is also taking a look at the 2nd document.

Lisa Christ
Chief, Targeting and Analysis Branch
Office of Ground Water and Drinking Water
202-564-8354

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 5/19/2020 4:59:30 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
CC: Khera, Rajiv [khera.rajiv@epa.gov]; Newcamp, Caitlin [Newcamp.Caitlin@epa.gov]; Alattar, Zaineb [alattar.zaineb@epa.gov]; Georges, Jessica [Georges.Jessica@epa.gov]; Huff, Lisa [Huff.Lisa@epa.gov]
Subject: FW: Notice of Final Action on Perchlorate
Attachments: Perchlorate Action Memo 5-19-20.docx; Draft Perchlorate Final Action FRN 5-19-20 v1.docx; Transmittal Memo JM to DR 5-18-20.docx

FYI only

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Tuesday, May 19, 2020 10:35 AM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Attached is a clean version of the notice with your edits accepted. Also attached is a clean version of the Action memo with the edits I sent you last night accepted. Lastly attached is the unchanged memo from you to Dave Ross.

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Tuesday, May 19, 2020 9:15 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Eric – I have made two minor edits in the attached. I will send this to Charlotte so that she can see how we've addressed her comments. At the same time we will submit formally to OW. Please send us the final clean versions of the memos and the action for that process.

Thanks much
Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, May 18, 2020 8:42 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Jennifer:
I don't believe a discussion is necessary. Edits and responses to the questions are in the attached. Please let us know if a revised clean version is needed.
Eric

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Monday, May 18, 2020 5:34 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>

Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: FW: Notice of Final Action on Perchlorate

Eric – please let me know if you want to discuss.

From: Bertrand, Charlotte <Bertrand.Charlotte@epa.gov>
Sent: Monday, May 18, 2020 5:29 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Braschayko, Kelley <braschayko.kelley@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Aguirre, Janita <Aguirre.Janita@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Thanks – couple of bubble box questions and then I had one redline edit I added to the Notice.

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Monday, May 18, 2020 3:01 PM
To: Bertrand, Charlotte <Bertrand.Charlotte@epa.gov>
Cc: Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Braschayko, Kelley <braschayko.kelley@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Aguirre, Janita <Aguirre.Janita@epa.gov>
Subject: FW: Notice of Final Action on Perchlorate

Charlotte – as agreed, I'm sending you the draft final perchlorate FRN for review. The redline includes the changes made since the FAR. I'm also including the draft Action Memo. Please let us know if your preference is to have these submitted to OW through CMS now or after you have reviewed. Let me know if you want to talk.

Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, May 18, 2020 2:48 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FW: Notice of Final Action on Perchlorate

Jennifer:

Attached for transmission to OW are revised versions of the FRN for the Perchlorate Final Action. There is both a clean and track changes version that includes edits made since initiating FAR (including the edits you asked for on Saturday and adding 3 more SAB recommendations to page 14 that were in the proposal but were not included in the draft we provided you on Friday). Also please find clean version of the transmittal memo from you to Dave Ross and the Action memo incorporating your edits.

Please note that there is also a redline version of the Action Memo for you to see the responses to your comments on the document. I do not recommend transmitting that memo to OW.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, May 18, 2020 2:18 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Hi Eric,

Attached are the revised Redline and Clean versions of the Perchlorate FR Notice. Once we are ready for OP's submittal to OMB let me know and I will provide a version that adheres to OP's file name formatting guidelines.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, May 18, 2020 1:14 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Sam

1. Change the title please. This was requested by OGC at Sr. Leadership levels.
2. Provide the same level of detail on the SAB recommendations as was included in the proposal.
3. I don't think the HRRCA text is necessary and do not want to add it at this stage since there are OGC edits that already make this clear.

Eric

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, May 18, 2020 12:41 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Hi Eric,

Here is a revised Redline of the document (from FAR). We had a few questions/issues for your consideration about the attached file. Specifically:,

1- Page #1, Notice Tittle: We did not accept the edits to the notice tittle. Because, the tittle of the notice was specifically crafted by OGC to capture the multiple actions EPA is taking. Suggest consulting with OGC before modifying this tittle.
2- Page #14, SAB Recommendations: SAB provided 4 main recommendations in 2013 but we only listed the first recommendation. Please advise if we should list all 4 recommendations here or not.

3- Page #26, Missing HRRCA Text: This language was offered by TAB in its 5-13-20 version of the draft FRN, but it did not show up in the version provided by OGWDW with Eric's & Jennifer's comments. We have inserted the language here for the reviewer's consideration. Please advise if we should keep it.

Once you provide your feedback, I will modify the redline version and also provide a Clean copy for transmittal.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, May 18, 2020 8:42 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: FW: Notice of Final Action on Perchlorate

Lisa and Sam
Attached are Jennifer's comments and edits on the draft FRN. I have responded to her questions in the attached and made some additional edits. Can you please get a revised clean version and another redline version that compares this document and the version that was distributed to FAR?
Thanks for your work on this.
Eric

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Saturday, May 16, 2020 11:39 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: RE: Notice of Final Action on Perchlorate

Looks very good. See p. 6 for my only concern w/the revisions.

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Friday, May 15, 2020 5:03 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: Notice of Final Action on Perchlorate

Jennifer

Attached for your approval and transmittal to the Office of Water for their approval and transmittal to the Office Policy for initiation of interagency review is a *Federal Register* notice titled: "Notice of Final Action on Perchlorate." Also attached for your review are a draft transmittal memo from you to the Assistant

Administrator of Water, a draft Action Memorandum and a track changes version of the FR notice that denotes the changes made as a result of Final Agency Review.

On February 11, 2011, the EPA published a determination to regulate perchlorate in drinking water (76 FR 7762). On June 26, 2019 (84 FR 30524), the EPA published the proposed National Primary Drinking Water Regulation for Perchlorate and requested public comments on multiple alternative actions, including withdrawing the 2011 determination to regulate perchlorate. The EPA received approximately 1,500 comments on the proposed rule. In the attached notice, the EPA is withdrawing the 2011 Regulatory Determination and is making a final determination not to regulate perchlorate based on the Agency's consideration of public comments and the best available information.

I recommend that you approve and transmit the attached notice to the Office of Water for their review, approval and transmission to the Office of Policy to initiate interagency review in accordance with Executive Order 12866. If you need additional information or have questions pertaining to any aspect of this notice, please call me or have your staff contact Samuel Hernandez at 202-564-1735.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 4/27/2020 4:20:44 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: RE: Response to comment document
Attachments: Consolidated Perchlorate Draft Comment Response Report 4-24-20 v2.docx

Hi Sam,
I've attached the draft with my edits and comments. I want to consolidate responses so that if revisions are needed we don't need to cascade through the entire document. For example our ID#1.1 is essentially the same as #10.1. We should point all comments to #1.1, so I revised #10.1. I created a guide for myself to make sure things were pointing to 1 overarching response (see below). There needs to be a global search ID #1.1 not #1.1. Also make sure there are periods after See comment response ID #X.X. There were a few missing. This needs to be a really quick turnaround if you need help ask Jessica.
Lisa

Comment response ID

#1.1	**Ex. 5 Deliberative Process (DP)**	
#1.7		
#1.16		
#2.1		
#2.6		
#3.1		
#4.1		
Page 5-1		
#5.1		
#5.2		
#6.1		
#6.7		
#7.1		
#8.6		
#8.7		
#10.4		
#10.5		

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Friday, April 24, 2020 9:10 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: Response to comment document

Hi Lisa,

Attached you will find the consolidated response to comment document. To make the review process easier in this stage, I decided to have a separate file that includes only Section 8 (Health Effects). I think it is easier this way because it is the largest section in the document and providing edits and comments on the lager document might impact the editorial format on other sections.

I have only received partial input from ORD, I told Lynn that I could not wait any longer for their input and that I would send the document forward for review and that I was leaving placeholders for their input. There are only a handful of comments pending. She is aware of our very aggressive schedule on perchlorate.

I will be working in the coming days with the team to make another QA of the document to make sure that any issues we find are captured in the next round of revisions. I am also working on the cover and front matter of the report.

Thank You
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 2/6/2020 4:04:03 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: FW: are you in today?
Attachments: Perchlorate reductions - format.cw.docx

Hi Sam,
Please update the MD PWS in the attached document.

Thanks-
Lisa

From: Wadlington, Christina <Wadlington.Christina@epa.gov>
Sent: Thursday, February 06, 2020 10:52 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: are you in today?

From: Christ, Lisa
Sent: Thursday, February 06, 2020 9:37 AM
To: Wadlington, Christina <Wadlington.Christina@epa.gov>
Subject: RE: are you in today?

Perfect -- TY

From: Wadlington, Christina <Wadlington.Christina@epa.gov>
Sent: Thursday, February 06, 2020 9:36 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: are you in today?

Yep, is COB today ok? I think I can do this morning, but just in case.

From: Christ, Lisa
Sent: Thursday, February 06, 2020 9:32 AM
To: Wadlington, Christina <Wadlington.Christina@epa.gov>
Subject: RE: are you in today?

Yes – and thanks so much. Do you have time for another one?

From: Wadlington, Christina <Wadlington.Christina@epa.gov>
Sent: Thursday, February 06, 2020 9:30 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: are you in today?

How's this?

From: Christ, Lisa
Sent: Thursday, February 06, 2020 8:55 AM
To: Wadlington, Christina <Wadlington.Christina@epa.gov>
Subject: RE: are you in today?

Trying to pretty up a couple of documents. I used the WORD template you provided, but could use a little help. I've attached my work in progress on the 1st document. It could use some icons, etc. Do you have time to help? The content is approved, so it's just formatting…

From: Wadlington, Christina <Wadlington.Christina@epa.gov>
Sent: Thursday, February 06, 2020 8:53 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: are you in today?

I'm working from home. What's up?

From: Christ, Lisa
Sent: Thursday, February 06, 2020 8:53 AM
To: Wadlington, Christina <Wadlington.Christina@epa.gov>
Subject: are you in today?

Lisa Christ
Chief, Targeting and Analysis Branch
Office of Ground Water and Drinking Water
202-564-8354

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 3/2/2020 8:17:02 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: FW: Draft Perchlorate Compendium HRRCA sections 8-1 to 8-4 rk
Attachments: Draft Perchlorate Compendium HRRCA sections 8-1 to 8-4 rk-lc.docx

Hi Sam,
I reviewed the responses Rajiv drafted for sections 8.3 and 8.4. I would like to send this to Pooja to get her feedback on the level of detail we're including in our responses. Do you have any concerns with me sharing this draft with Pooja?
Thanks,
Lisa

From: Khera, Rajiv <Khera.Rajiv@epa.gov>
Sent: Tuesday, February 25, 2020 3:28 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: Draft Perchlorate Compendium HRRCA sections 8-1 to 8-4 rk

Hi Sam-The attached has responses to all HRRCA and Treatment comments (sections 8.3 and 8.4) including a general response for the entire HRRCA section (start of 8.3) and responses to a few additional non-HRRCA sections (see comments 8.1 and 9.13). Part of some of our responses need to be cross referenced to other responses that are being developed by other team members, so for now those parts have been highlighted. Let me know if you have any questions. Thanks
Rajiv

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 2/6/2020 2:31:58 PM
To: Wadlington, Christina [Wadlington.Christina@epa.gov]
Subject: RE: are you in today?
Attachments: Perchlorate reductions - format.docx

Yes – and thanks so much. Do you have time for another one?

From: Wadlington, Christina <Wadlington.Christina@epa.gov>
Sent: Thursday, February 06, 2020 9:30 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: are you in today?

How's this?

From: Christ, Lisa
Sent: Thursday, February 06, 2020 8:55 AM
To: Wadlington, Christina <Wadlington.Christina@epa.gov>
Subject: RE: are you in today?

Trying to pretty up a couple of documents. I used the WORD template you provided, but could use a little help. I've attached my work in progress on the 1st document. It could use some icons, etc. Do you have time to help? The content is approved, so it's just formatting…

From: Wadlington, Christina <Wadlington.Christina@epa.gov>
Sent: Thursday, February 06, 2020 8:53 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: are you in today?

I'm working from home. What's up?

From: Christ, Lisa
Sent: Thursday, February 06, 2020 8:53 AM
To: Wadlington, Christina <Wadlington.Christina@epa.gov>
Subject: are you in today?

Lisa Christ
Chief, Targeting and Analysis Branch
Office of Ground Water and Drinking Water
202-564-8354

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 3/16/2020 9:16:30 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: RE: EDITS - RE: Revised Perchlorate Briefing Documents
Attachments: Perchlorate Reductions_03.16.2020-lc.docx

Forgot to provide my input

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, March 16, 2020 4:50 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: EDITS - RE: Revised Perchlorate Briefing Documents

Hi Lisa,

I was able to get the information from an older email I had.

If you can send the introduction writeup I can fold that into the revised version.

Also, I am unable to see exactly what are the comments or questions on the Recommendations document. Do you know what the highlight means?

Thanks
Sam

==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Monday, March 16, 2020 4:02 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: EDITS - RE: Revised Perchlorate Briefing Documents

Thanks Sam
The studies may be in the docket if they are referenced in the occurrence support document.
Lisa

Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Monday, March 16, 2020 3:47 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: EDITS - RE: Revised Perchlorate Briefing Documents

Hi Lisa,

I am looking at these right now.

On a related note, I am having issues assessing my Perchlorate files on the Network. These reports from the occurrence analysis are in my network drive folders which I am unable to access. I will try again later tonight to see if lower network traffic lets me go in.

If I am unable to do so, I will have to go to the office to download my network drive to my Laptop, I will keep you posted.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Monday, March 16, 2020 3:37 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FW: EDITS - RE: Revised Perchlorate Briefing Documents

Hi Sam,
Please take a a look at the comments and let me know if you think any are significant. I can prepare the intro to the reductions document. I don't know if we have the actual study results for AZ and NV –I feel like we've been asked this before. Let me know if you have questions.
Lisa

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, March 16, 2020 3:02 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FW: EDITS - RE: Revised Perchlorate Briefing Documents

Lisa:
Please take a look at the comments/ revisions in the attached and let me know if you would like to have a call to discuss how to incorporate these changes.
Eric

From: Tiago, Joseph <Tiago.Joseph@epa.gov>
Sent: Monday, March 16, 2020 2:53 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Cc: McLain, Jennifer L. <McLain.Jennifer@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Subject: FW: EDITS - RE: Revised Perchlorate Briefing Documents

From: Aguirre, Janita <Aguirre.Janita@epa.gov>
Sent: Monday, March 16, 2020 2:49 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>
Subject: EDITS - RE: Revised Perchlorate Briefing Documents
Importance: High

Hi Jennifer,

A few edits from Dave. Please review and confirm. In particular, please address the comment bubbles in the "Perchlorate Reductions" document. Please also review the write-up under #4 in the "Perchlorate Recommendations for PWS" document to confirm that it uses guidance type language, rather than authoritative, regulatory language. Due to formatting, yellow highlights (rather than redline) show changed text.

This is due tomorrow by noon, so please let me know as soon as the edits are incorporated.

Thank you,
Janita

Janita Aguirre – Special Assistant to David Ross and Anna Wildeman
U.S. Environmental Protection Agency | Office of Water | Office of the Assistant Administrator
Phone: **(202) 566-1149** | Email: **aguirre.janita@epa.gov**

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Friday, March 13, 2020 5:34 PM
To: Aguirre, Janita <Aguirre.Janita@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>
Subject: FW: Revised Perchlorate Briefing Documents

Janita – your assistance on this is appreciated! Is it possible to provide these revised documents – updated per Dave's input?

Thank you
Jennifer

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Friday, March 13, 2020 5:28 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>
Subject: Revised Perchlorate Briefing Documents

Jennifer:
Attached please find a revised Perchlorate Briefing documents. We had submitted a previous versions of these document for OW review along with the Perchlorate Reductions and Recommendations Documents. We have updated these documents while awaiting further comments from OW. The revisions made to the documents are as follows

- The one pager – Decision for Perchlorate Final Regulatory Action – Has been updated in response to Dave's request to incorporate information about the timing of the release of the stipulation to NRDC regarding the consent decree. This document reflects OGC's input.
- The Reductions Document – has been updated to reflect the information we received from the States of Maryland and Ohio regarding the status of the system that previously detected perchlorate at levels greater than 18ppb. We have also added a document number.
- The Recommendations Document has been updated to reflect add a Document Number.

If OW has not yet reviewed the last versions provided we recommend sending these forward to replace the versions awaiting review. If there are comments on the previous versions we can incorporate those prior to sending them forward.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 2/25/2020 5:27:38 PM
To: Alattar, Zaineb [alattar.zaineb@epa.gov]
Subject: FW: Perchlorate Team Meeting
Attachments: Draft Perchlorate Compendium.docx; LF Fact Sheet.docx

Hi Zaineb,
This is the version of the comment compendium I have. Also attached is the draft LF fact sheet. It could use some help!

Lisa

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Wednesday, January 15, 2020 10:16 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: FW: Perchlorate Team Meeting

FYI.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Hernandez-Quinones, Samuel
Sent: Monday, December 09, 2019 11:02 AM
To: Miller, Gregory <Miller.Gregory@epa.gov>
Subject: RE: Perchlorate Team Meeting

Ok, we can have a call later in the week.

Also, I am attaching here a copy of the draft compendium of comments for Perchlorate. I think you will be interested in seeing the comments on section 8.1. Let me know if you have any questions.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW

Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

-----Original Appointment-----
From: Miller, Gregory <Miller.Gregory@epa.gov>
Sent: Monday, December 09, 2019 7:28 AM
To: Hernandez-Quinones, Samuel
Subject: Tentative: Perchlorate Team Meeting
When: Wednesday, December 11, 2019 2:00 PM-2:45 PM (UTC-05:00) Eastern Time (US & Canada).
Where: DCRoomEast2406/DC-ICC-OW-OGWDW

Hi Sam,
I'm not going to be available for this meeting. I'll give you a call to check in. Thanks.

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 9/11/2019 8:18:12 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: FW: draft summary of perchlorate public comments -- Eric was wondering when this would be ready?
Attachments: Perchlorate Comment Summary V3.docx

Importance: High

From: Christ, Lisa
Sent: Wednesday, September 11, 2019 12:02 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FW: draft summary of perchlorate public comments

Hi Sam,
Please see Eric's request below. I think he'd like to share with OW on Friday.

Thanks,
Lisa

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Wednesday, September 11, 2019 12:00 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: draft summary of perchlorate public comments

Thanks Lisa this breakdown is helpful but it pointed out to me that the 109 extensive and substantive letters don't all appear to be summarized.
I think there isn't a need to organize the commenters by organization type and there are some groups that are hard to categorize (i.e. we have ACWA as a regulated stakeholder but AWWA is a trade organization when the both represent drinking water utilities) I also think there is redundancy in the summary of the comments that I tried to eliminate in the attached.
Can the team take a look and see if there are organizations that have submitted extensive and substantive comments that we have not listed and if so please list them in the categories of support that are in the attached.

From: Christ, Lisa
Sent: Wednesday, September 11, 2019 7:46 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Subject: FW: draft summary of perchlorate public comments

Revised

From: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Sent: Tuesday, September 10, 2019 4:04 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: RE: draft summary of perchlorate public comments

Hi Lisa,

Here is a revised version which incorporates previously suggested edits.

- We received 6 comment letters in support of the proposed rule at 56 ppb.
- I cannot categorically confirm that the mass mailing campaign was organized by any group, so I am removing that designation from the summary document.
- From the individual substantive letters
    - 1 supports withdrawal option
    - 1 supports 90 ppb option
    - 6 support 18 ppb option
    - 23 support regulation at a stricter level than 18pbb

Thanks
Sam

==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Tuesday, September 10, 2019 1:44 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FW: draft summary of perchlorate public comments

Hi Sam,
As follow up can you please:

- Confirm we did not get support for regulation at 56 ppb
- Confirm if NRDC is mentioned as the originator of the mass campaign
- Count the 88 individual comments that 1- support withdrawal, 2- support regulation (at any concentration).

Let me know if you have questions
Thanks,
Lisa

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Tuesday, September 10, 2019 1:30 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>; Lombardi, Thomas <lombardi.thomas@epa.gov>; Alattar, Zaineb <alattar.zaineb@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: RE: draft summary of perchlorate public comments

Also There are three categories of commenters presented

1. Support withdrawal
2. Support a stricter than proposed standard
3. Neutral

Does this mean there were no commenters in support of the proposed MCLG/MCL?

From: Burneson, Eric
Sent: Tuesday, September 10, 2019 1:27 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>; Lombardi, Thomas <lombardi.thomas@epa.gov>; Alattar, Zaineb <alattar.zaineb@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: RE: draft summary of perchlorate public comments

Thanks Lisa: My only comment is that unless the comment campaign letters clearly state they are submitting comments organized by NRDC or there is public information from NRDC clearly stating that they organized a comment campaign we should not attribute the campaign to them.
Eric

From: Christ, Lisa
Sent: Tuesday, September 10, 2019 12:27 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Newcamp, Caitlin <Newcamp.Caitlin@epa.gov>; Lombardi, Thomas <lombardi.thomas@epa.gov>; Alattar, Zaineb <alattar.zaineb@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>
Subject: draft summary of perchlorate public comments

Eric,
Attached is a high level summary of the public comments received on the perchlorate proposal. OGC requested a summary to prepare the notice to the court requesting an extension of the consent decree final rule deadline. Let me know if you have questions or would like to discuss.
Lisa

Lisa Christ
Chief, Targeting and Analysis Branch
Office of Ground Water and Drinking Water
202-564-8354

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 1/29/2020 4:59:14 PM
To: McLain, Jennifer L. [Mclain.Jennifer@epa.gov]
CC: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]; Huff, Lisa [Huff.Lisa@epa.gov]; Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]
Subject: FOR REVIEW: perchlorate reductions & PWS recommendations
Attachments: Perchlorate Recommendations for PWS 1-28-20 Ver2.docx; Redline - Perchlorate Recommendations for PWS 1-28-20 Ver2.docx; Reductions of Perchlorate in Drinking Water 1-29-2020.docx; Redline - Reductions of Perchlorate in Drinking Water 1-29-2020.docx

Hi Jennifer,
The attached documents incorporate edits/address comments from you, Christina and Pooja. There are clean and track change versions. Let us know if you have questions, etc.
Thank you,

Lisa

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 5/14/2020 2:59:31 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: FW: FOR REVIEW: draft perchlorate action and transmittal memos
Attachments: Transmittal Memo JM to DR 5-13-20 v1.SF.docx; Perchlorate Action Memo 5-13-2020_.SF.docx

Hi Sam – I'll work on revising the memos so you can focus on the RTC document.

Lisa

From: Flaharty, Stephanie <Flaharty.Stephanie@epa.gov>
Sent: Thursday, May 14, 2020 10:54 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: FOR REVIEW: draft perchlorate action and transmittal memos

Hi Lisa,

The attached drafts reflect formatting edits (Dave's preferences and OP's template).

I noted in the Action Memo file that the updated section, now titled "STAKEHOLDER INVOLVEMENT and ANTICIPATED RESPONSE," prompts the lead office to discuss any *stakeholder involvement that occurred during development of the action.*

Thanks for checking…

Best,
Steph

From: Flaharty, Stephanie
Sent: Thursday, May 14, 2020 7:55 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: FOR REVIEW: draft perchlorate action and transmittal memos

Good Morning Lisa,

I'm going to have quite a few edits (per Dave's preferred format) and will send you the drafts a bit later this morning.

Thanks,
Steph

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Wednesday, May 13, 2020 4:25 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>

Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Flaharty, Stephanie <Flaharty.Stephanie@epa.gov>
Subject: RE: FOR REVIEW: draft perchlorate action and transmittal memos

Lisa:
Attached please find my suggested edits to the Perchlorate transmittal memo and action memo. I modified the memos to reflect our status of submission to OMB for Interagency review.
I am copying Stephanie so that she may provide any additional edits to assure consistency with Agency templates.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

From: Christ, Lisa <Christ.Lisa@epa.gov>
Sent: Wednesday, May 06, 2020 3:51 PM
To: Burneson, Eric <Burneson.Eric@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: FOR REVIEW: draft perchlorate action and transmittal memos

DRAFT DELIVERABLE
Hi Eric,
For you review are the draft memos to accompany the perchlorate final action. Please let us know if you have question, concerns or need more information.
Thanks,
Lisa

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 4/20/2020 1:53:17 PM
To: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: FW: Perchlorate FRN For your Review
Attachments: Draft Perchlorate Reg Det Withdrawal FR Notice 4-13-20 v2.2 Clean.ogwdw.docx; Perchlorate Action Memo 4-13-2020.docx; Perchlorate Draft Comment Response Report - Lisa C Review 4-15-20-.docx

Hi Sam,
Good morning. Attached are Jennifer's comments on the FRN which are pretty straight forward. I've also attached the action memo and response to comment section with my comments. Next steps:
Prepare revised FRN and memos for IO review and transmittal to Dave today.
Compile the RTC document so I can do a complete start-to-finish review for consistency, etc. We'll need to get this to Eric this week.

Thanks – let me know if you have questions or concerns.
Lisa

From: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Sent: Saturday, April 18, 2020 9:34 AM
To: Burneson, Eric <Burneson.Eric@epa.gov>
Cc: Tiago, Joseph <Tiago.Joseph@epa.gov>; Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Wehling, Carrie <Wehling.Carrie@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Parikh, Pooja <Parikh.Pooja@epa.gov>
Subject: RE: Perchlorate FRN For your Review

Here are my comments on the FRN. Sorry it took so long. It looks great! Thanks much to Lisa, Sam and the TAB and WLO teams for once again doing such high quality work. It certainly makes my review much easier.

Ex. 5 Deliberative Process (DP)

Jennifer

deliberative

From: Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>
Sent: Tuesday, April 14, 2020 5:48 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Subject: RE: Perchlorate FRN For your Review

A few changes in the attached file for your consideration. Thanks.

Yu-Ting Guilaran, P.E.

Deputy Office Director
Office of Ground Water and Drinking Water
Office of Water
U.S. Environmental Protection Agency
Mail code: 4601M

Tel: 202-564-6591

From: Burneson, Eric <Burneson.Eric@epa.gov>
Sent: Monday, April 13, 2020 7:27 PM
To: McLain, Jennifer L. <McLain.Jennifer@epa.gov>
Cc: Guilaran, Yu-Ting <Guilaran.Yu-Ting@epa.gov>; Wehling, Carrie <Wehling.Carrie@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Parikh, Pooja <Parikh.Pooja@epa.gov>
Subject: Perchlorate FRN For your Review

Jennifer:
Attached please find for your review a draft FR notice for the withdrawal of the regulatory determination. As discussed our goal is to initiate an expedited FAR For this notice next week. The attached incorporates input from OGC and I am copying Carrie and Pooja so that they can coordinate with their front office as necessary prior to FAR. I will update you on the status of our Response to Comment Document tomorrow. Thanks in advance for your input.

Eric Burneson, P.E.
Director of Standards and Risk Management
Office of Ground Water and Drinking Water
U.S. Environmental Protection Agency
202 564 5250

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 12/20/2019 3:37:54 PM
To: Khera, Rajiv [Khera.Rajiv@epa.gov]
CC: Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: RE: Let me know if you want me to call in for the meeting at 4PM
Attachments: Option Selection for Perchlorate 12-20-19.docx

Hi Rajiv,
I updated the briefing document to incorporate the new assumptions. Please use the attached to include the new analysis.

Let me know if you have questions or if the below isn't clear.

Thanks!
Lisa

From: Christ, Lisa
Sent: Thursday, December 19, 2019 5:03 PM
To: Khera, Rajiv <Khera.Rajiv@epa.gov>
Cc: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: RE: Let me know if you want me to call in for the meeting at 4PM

Hi Rajiv,
Sorry I didn't see this sooner! Eric suggested that we use different assumptions for the spring-in option. Rather than look at the state level, assume that all states will not require any monitoring for any system that had non-detect in UCMR1 and that any system with detects or that did not have data from UCMR1 (smalls) the state would make a case-by-case decision. Assume that the burden for the case-by-case system evaluation would be more burden hours than the waiver process. This can wait until you are back after the holidays.

Lisa

From: Khera, Rajiv <Khera.Rajiv@epa.gov>
Sent: Thursday, December 19, 2019 3:51 PM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: Let me know if you want me to call in for the meeting at 4PM

Thanks!

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 2/7/2019 9:00:13 PM
To: Rodgers-Jenkins, Crystal [Rodgers-Jenkins.Crystal@epa.gov]
CC: Huff, Lisa [Huff.Lisa@epa.gov]
Subject: FW: Excepted Contract List (PLANNING EXERCISE ONLY) Due NLT February 8, 2019
Attachments: Copy of Excepted Contracts List tab 2-5-2019.xlsx

Hi Crystal,
The attached spreadsheet contains the revisions we walked through during today's TAB updates.
Thanks-
Lisa

From: Bissonette, Eric
Sent: Friday, February 01, 2019 7:35 AM
To: Travers, David <Travers.David@epa.gov>; Newberry, Debbie <Newberry.Debbie@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>; Albert, Ryan <Albert.Ryan@epa.gov>; Carroll, Gregory <Carroll.Gregory@epa.gov>; Hautman, Dan <Hautman.Dan@epa.gov>; Workman, Rosemary <Workman.Rosemary@epa.gov>; Tidwell-Shelton, Patricia <Tidwell-Shelton.Patricia@epa.gov>; Thompkins, Anita <Thompkins.Anita@epa.gov>; Corr, Elizabeth <Corr.Elizabeth@epa.gov>; Bergman, Ronald <Bergman.Ronald@epa.gov>; Plastino, Michael <Plastino.Michael@epa.gov>; Fort, Felecia <Fort.Felecia@epa.gov>; Bates, William <bates.william@epa.gov>; Tierney, Meghan <Tierney.Meghan@epa.gov>; Lopez-Carbo, Maria <Lopez-Carbo.Maria@epa.gov>; Davis, CatherineM <Davis.CatherineM@epa.gov>
Cc: Mclain, Jennifer <Mclain.Jennifer@epa.gov>; Cooper, Tiffany <Cooper.Tiffany@epa.gov>; Parrotta, Nancy <Parrotta.Nancy@epa.gov>; Keyton, Lori <Keyton.Lori@epa.gov>
Subject: Excepted Contract List (PLANNING EXERCISE ONLY) Due NLT February 8, 2019

Attached you will find the *Excepted Contracts List*, as of January 10th. Please begin taking inventory to make early determinations if additional contracts/Work Assignments/Task Orders should be added. When reviewing the attached spreadsheet, please be sure to make the necessary updates to your excepted contract justifications so they are better aligned with the definition of "excepted activities."

Examples of excepted activities relevant to the Agency cited in the OMB guidance include:

- Activities essential to ensure against an imminent threat to public health and safety, including safe use of food and drugs, and safe use of hazardous materials;
- Protection of Federal lands, buildings, waterways, equipment and other property owned by the Government;
- Law enforcement and criminal investigation;
- Emergency and disaster assistance and;
- Activities necessary to maintain protection of research property, including data

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 2/4/2019 9:53:18 PM
To: Helm, Erik [helm.erik@epa.gov]; Khera, Rajiv [khera.rajiv@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
CC: Huff, Lisa [Huff.Lisa@epa.gov]
Subject: FW: Excepted Contract List (PLANNING EXERCISE ONLY) Due NLT February 8, 2019
Attachments: Excepted Contracts List Dec 01-10-2019 646pm revised format.xlsx

Hi All,
I'm checking to make sure our Cadmus and Abt work continues in the event of another shutdown. Can you confirm that the listed WAs are complete and we don't need to add? OR remove?

OP Abt contract [EP-W-17-009] we have WAs 2-15 and 2-22 (LCR) and WA 2-19 (perchlorate)
Cadmus [EP-C-12-023] WA 6-08 (LCR) and WA 6-29 (perchlorate)
BPA Abt contract [EP-BPA-16-C-0001] TOs 68HE0C18Q0177 and 68HE0C18F0044 (perchlorate) and EP-817C-00023 (LCR)

Thanks!
Lisa

From: Bissonette, Eric
Sent: Friday, February 01, 2019 7:35 AM
To: Travers, David <Travers.David@epa.gov>; Newberry, Debbie <Newberry.Debbie@epa.gov>; Burneson, Eric <Burneson.Eric@epa.gov>; Rodgers-Jenkins, Crystal <Rodgers-Jenkins.Crystal@epa.gov>; Christ, Lisa <Christ.Lisa@epa.gov>; Huff, Lisa <Huff.Lisa@epa.gov>; Albert, Ryan <Albert.Ryan@epa.gov>; Carroll, Gregory <Carroll.Gregory@epa.gov>; Hautman, Dan <Hautman.Dan@epa.gov>; Workman, Rosemary <Workman.Rosemary@epa.gov>; Tidwell-Shelton, Patricia <Tidwell-Shelton.Patricia@epa.gov>; Thompkins, Anita <Thompkins.Anita@epa.gov>; Corr, Elizabeth <Corr.Elizabeth@epa.gov>; Bergman, Ronald <Bergman.Ronald@epa.gov>; Plastino, Michael <Plastino.Michael@epa.gov>; Fort, Felecia <Fort.Felecia@epa.gov>; Bates, William <bates.william@epa.gov>; Tierney, Meghan <Tierney.Meghan@epa.gov>; Lopez-Carbo, Maria <Lopez-Carbo.Maria@epa.gov>; Davis, CatherineM <Davis.CatherineM@epa.gov>
Cc: Mclain, Jennifer <Mclain.Jennifer@epa.gov>; Cooper, Tiffany <Cooper.Tiffany@epa.gov>; Parrotta, Nancy <Parrotta.Nancy@epa.gov>; Keyton, Lori <Keyton.Lori@epa.gov>
Subject: Excepted Contract List (PLANNING EXERCISE ONLY) Due NLT February 8, 2019

Attached you will find the *Excepted Contracts List*, as of January 10th. Please begin taking inventory to make early determinations if additional contracts/Work Assignments/Task Orders should be added. When reviewing the attached spreadsheet, please be sure to make the necessary updates to your excepted contract justifications so they are better aligned with the definition of "excepted activities."

Examples of excepted activities relevant to the Agency cited in the OMB guidance include:

- Activities essential to ensure against an imminent threat to public health and safety, including safe use of food and drugs, and safe use of hazardous materials;
- Protection of Federal lands, buildings, waterways, equipment and other property owned by the Government;
- Law enforcement and criminal investigation;
- Emergency and disaster assistance and;

- Activities necessary to maintain protection of research property, including data

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 2/4/2019 9:30:32 PM
To: Flaharty, Stephanie [Flaharty.Stephanie@epa.gov]
Subject: FW: Technical Support Documents - Draft Perchlorate Rule Proposal
Attachments: 181129_DRAFT MCLG TSD.DOCX; Draft Perchlorate HRRCA 2019-02-03.docx; PerchlorateOccMonitoringReport_Updated 2-1-19.docx; Perchlorate T&C November 2018.docx; Perchlorate BAT and SSCT November 2018.docx; WA459_T4_Vol1 Main Report_181113.docx

FYI only –

From: Hernandez-Quinones, Samuel
Sent: Monday, February 04, 2019 3:55 PM
To: Johnson, Ann <Johnson.Ann@epa.gov>; Dockins, Chris <Dockins.Chris@epa.gov>; Shao, Nicole <Shao.Nicole@epa.gov>; Miller, Gregory <Miller.Gregory@epa.gov>; Flowers, Lynn <Flowers.Lynn@epa.gov>; Foster, Stiven <Foster.Stiven@epa.gov>; Kyprianou, Rose <Kyprianou.Rose@epa.gov>; Miller, Wynne <Miller.Wynne@epa.gov>; Raffaele, Kathleen <raffaele.kathleen@epa.gov>
Cc: Christ, Lisa <Christ.Lisa@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: Technical Support Documents - Draft Perchlorate Rule Proposal

Preliminary draft for internal EPA review

Hi,

Attached are copies of the draft technical support documents that were used as basis for the Perchlorate Rule Proposal. As mentioned earlier today we are not requesting comments on these documents within the two-week review time frame.

Economic Analysis
MCLG Derivation Document
Treatment Technologies & Costs Document
Occurrence & Monitoring Report
MCLG Approaches Document
Best Available Technologies Document

Thanks
Sam

==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

From: Hernandez-Quinones, Samuel
Sent: Monday, February 04, 2019 10:32 AM
To: Cc: Christ, Lisa <christ.lisa@epa.gov>; Burneson, Eric <burneson.eric@epa.gov>; Flaharty, Stephanie <Flaharty.Stephanie@epa.gov>; Messier, Dawn <Messier.Dawn@epa.gov>; Wehling, Carrie <Wehling.Carrie@epa.gov>;

Huff, Lisa <Huff.Lisa@epa.gov>; Khera, Rajiv <Khera.Rajiv@epa.gov>
Subject: Request for review - Draft Perchlorate Rule Proposal

Preliminary draft for internal EPA review

Hi,

Attached for your review is the Draft Perchlorate Rule Proposal (Preamble and Regulatory Text). As discussed previously we are asking that you provide your questions and or comments on the draft document to me by COB 2/15/2019. In order to keep with the consent decree deadline, we need to complete this step of the process within two weeks, if there are any issues that require technical discussions please let me know so that we can arrange any necessary working meeting.

I will follow-up with another email later today that contains the draft version of the technical support documents that were used as the basis for the Perchlorate proposal. Since those are very lengthy documents we are not requesting that you submit input and/or comments on those within the two- week time frame.

Please let me know if you have any questions.

Thanks
Sam
==========
Samuel Hernández Quiñones, P.E.
Environmental Engineer
Office of Water
Environmental Protection Agency
1200 Pennsylvania Ave. NW
Washington, DC 20460
202-564-1735

"USEPA Protecting Human Health and the Environment"

Message

From: Christ, Lisa [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=10DBD8E424704E43B5A50F74A4DAC626-LCHRIST]
Sent: 11/9/2018 7:48:34 PM
To: Khera, Rajiv [khera.rajiv@epa.gov]; Hernandez-Quinones, Samuel [Hernandez.Samuel@epa.gov]
Subject: FW: Perchlorate preamble draft
Attachments: TREAT12 Preamble 101818-lc.docx

Gentlemen,
Please find attached my comments on the draft FRN. Sam, you'll need to compile these with my previous comments on the other version of the FRN.
Let's meet next week to plan completion of the FRN and technical support documents.

Thanks-
Lisa

From: Khera, Rajiv
Sent: Thursday, November 08, 2018 7:59 AM
To: Christ, Lisa <Christ.Lisa@epa.gov>
Subject: Perchlorate preamble draft

From: Khera, Rajiv
Sent: Wednesday, November 07, 2018 12:45 PM
To: Hernandez-Quinones, Samuel <Hernandez.Samuel@epa.gov>
Subject: Perchlorate preamble draft

Sam,

Attached is the latest draft of the Perchlorate preamble. It has the following sections:

Health effects
Proposed MCLG
Occurrence
Treatment (BAT subsections may need more treatment detail especially any limitations to use)
Economic analysis methods and results (the benefits section needs more detail; I am wondering if we should include the equations?)
Executive Orders (there are highlights on text about things I don't know like outreach/consultation and gray highlights on values that may change).

Hope you will find this useful. Thanks

Rajiv